



TCACGTA AAA AGGTA TACTA GAATTATGAT GATTACTCTG CGCAAACTTC CTCTGGCGGT TGCCGTGCGA GCGGCGCTAA TGTCTGCTCA GGCCATGGCC
AGTGCATTTT TCCCATAGAT CTTAATACTA CTAATGAGAC GCGTTTGAAG GAGACGCGCA ACGGACGCTT CCGCCGCAAT ACAGACGAGT CCGGTACCGG
MetMe tIleThrLeu ArgLysLeuP roLeuAlaValAla AlaGlyValM etSerAlaG1 nAlaMetAla
^Start of lamB signal sequence

GGTCCGAAA CTCTGTGCGG TGTGAACCTG GTTGACGCTC TGCAGTTCTG ATCTGGTGAT CGAGGCTTCC TGTTCAACAA ACCGACTGGG GCTGGATCCT
CCAGGCTTT GAGACAGCC ACGACTTGAC CAACCTGCGAG ACGTCAAGCA TACACCACTA GCTCCGAAAG ACAAGTTGTT TGGCTGACCC CGACCTAGGA
GlyProGluT hrLeuCysG1 yAlaGluLeu ValAspAlaL euGlnPheVa lCysGlyAsp ArgGlyPheL euPheasnLy sProThrGly AlaGlySerSer
^Start of IGF-I (Y24L, Y31A)

CCTCTCGTCG TGCTCCCCAG ACTGGTATTG TTGACGAATG CTGCTTTCTG TCTTGGGACC TGGCTCGTCT GGAAATGTAT TGGGCTCCCC TGAACACCGC
GGAGAGCAGC ACGAGGGGTC TGACCATTAAC AACTGCTTAC GACGAAAGCA AGAACGCTGG ACGCAGCAGA CCTTTACATA ACGGAGGGG ACTTTGGGCG
SerArgar galProGln ThrGlyIleV alaspGluCy sCysPheArg SerCysAspL euArgArgLe uGluMetTyr CysAlaProL euLysProAla

TAAATCTGCT TAGAAGCTCC TAACGCTCGG TTGCCGCCGG GCGTTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG
ATTTAGACGA ATCTTCGAGG ATTGCGAGCC AACGGCGGCC CGCAAAAAT AACAAATTGAG TACAAACTGT CGAATAGTAG CTATTTCGAA TTACGCCATC
LysSerAla Am*

Nucleotide and Amino Acid Sequence of the LamB Signal Sequence and IGF-I (Y24L, Y31A)

FIG. 1

09724157

6693079

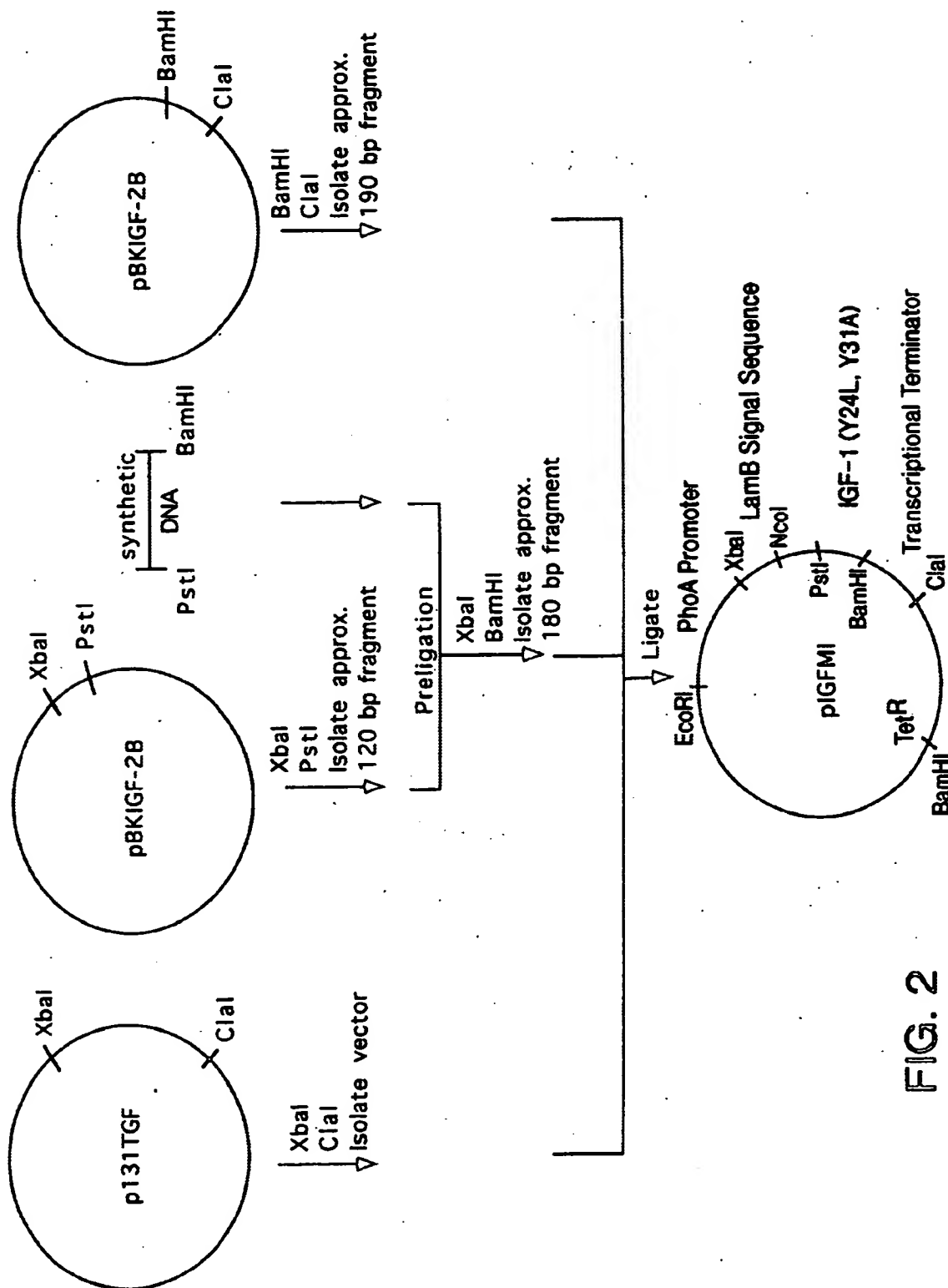


FIG. 2





plasmid IGfMI
length: 5115 (circular)

1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAATAATC TCATTGCTGA GTTGTATATT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA
101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGGC GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTACGA AGGTTATAC CGCGTTTAC TGGTTGTGCG CAACATACTA GTCCATCTCC
201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCCTGA CGACGATACG GAGTGTCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTACGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT
301 AAAAGTTAAT CTTTTCACCA GCTGTCAATA AGTTGTACG GCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTTGTAACATA GTACGCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CCGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA
401 TCACGTAAAA AGGGTATCTA GAATTATGAT GATTACTCTG CGCAAACTTC CTCGTGCGGT TGCGGCGTAA TGCTGTCTCA GGCATGGGCC
AGTGCAATTT TCCCATAGAT CTTAATACTA CTAATGAGAC GCGTTTGAAG GAGACCGCA ACGGACGCT CGCCCGCAT ACAGACGAGT CCGGTACCGG
1 MetMe tileThrLeu ArgLysLeup roLeuAlaAla lAlaValAla AlaglyValM etSerAlaGl nAlaMetAla
501 GGTCCCGAAA CTCGTGCGG TGCTGAACCTG GTTGACGCTC TGAGTTCGT ATGTGCTGAT CGAGGCTTCC TGTTCAACAA ACCGACTGGG GCTGATCTCT
CCAGGCTTT GAGACACGCC ACGACTTGAC CAACCTGCGAG ACGTCAAGCA TACACCACTA GCTCCGAAGG ACAAGTTGTT TGCGTGACCC CGACTTAGGA
26 GlyProGlu hrLeuCysG1 yAlaGluLeu ValAspAlaL euGlnPheVa lCysGlyAsp ArgGlyPheL eupheAsnLy sProThrGly AlaglySerSer
601 CCTCTCGTCG TGCTCCCCAG ACTGGTATTG TTGACGAATG CTGCTTTCGT TCTTGCGACC TGCGTCGTCT GGAATGTAT TGCGTCCCC TGAAACCCCG
GGAGAGCAGC ACGAGGGGTC TGACCATAC AACTGCTTAC GACGAAAGCA AGAACGCTGG ACGCAGCAGA CCTTTACATA ACGGAGGGG ACTTTGGGCG
60 SerArgAr gAlaProGln ThrGlyIlev alaSpGlucy sCysPheArg SerCysAspL euArgArgLe uGluMetTyr CysAlaProL euLysProAla
701 TAAATCTGCT TAGAAGCTCC TAAAGCTCGG TTGCGCGCCCG GCGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG
ATTAGACGA ATCTTCGAGG ATTGCGAGCC AACGCGCGCC CGCAAAAT TACAATTCAG TACAACCTGT CGAATAGTAG CTATTGAAA TTACGCCATC
93 LysSerAla Am*
801 TTTATCACAG TTAATTTGCT AACGCAGTCA GGCACCGTGT ATGAATCTA ACAATGCGCT CATCGTCATC CTCGGCACCG TCACCCCTGGA TGCTGTAGGC
AAATAGTGC AATTAAACGA TTGCGTCAGT CCGTGGCACA TACTTTAGAT TGTACGCGA GTAGCAGTAG GAGCCGTGGC AGTGGACCT ACGACATCCG
901 ATAGGCTTGG TTATGCCGGT ACTGCCGGG CTCTTGGGGA ATATCGTCCA TTCCGACAGC ATGCCAGTC ACTATGGCGT GCTGTAGCG CTATATGCGT
TATCCGAACC AATACGGCCA TGACGCGCCG GAGAACGCC TATAGCAGT AAGCTGTG TAGCGGTGAG TGATACCGCA CGACGATCGC GATATACGCA
1001 TGATGCAATT TCTATGCGCA CCCGTTCTCG GAGCACTGTC CGACCGCTTT GCGCGCGGCC CAGTCTCTGCT CGCTTCGCTA CTTGGAGCCA CTATCGACTA
ACTACGTTAA AGATACGCGT GGCACAGAGC CTCGTGACAG GCTGGCGAAA CCGCGGCGG GTCAGGACGA GCGAAGCGAT GAACCTCGGT GATAGCTGAT

FIG. 3A

[illegible]

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2501 AGTGATTTT CTCTGGTCCC TACCGCCAGT TGTTTACCT CACACGCTTC CAGTAACCGG GCATGTTTCAT CATCAGTAAC CCGTATCGTG
TCACATAAAA GAGACCAGG CGCGGTAGGT ATGGCGGTCA ACAAATGGGA GTGTTGCAAG GTCATTGGCC CGTACNAGTA GTAGTCATTG GGCATAGCAC

2601 AGCATCCTCT CTCGTTTCAT CCGTATCATT ACCCCCATGA ACAGAAATTC CCCCTTACAC GGAGGCATCA AGTGACCAA CAGGAAAAAA CCGCCCTTAA
TCGTAGGAGA GAGCAAGTA GCCATAGTAA TGGGGTACT TGCTTTAAG GGGGATCTG CCTCCGTAGT TCACTGGTTT GTCCCTTTT GCGGGAAAT

2701 CATGGCCCG TTTATCAGAA GCCAGACATT AACGCTTCTG AGGAGCTGA ACGGATGAA CCGGATGAA CAGGCAGACA TCTGTGAATC GCTTCACGAC
GTACCGGGCG AATAGTCTT CCGTCTGTAA TTGGAAGAC CTCCTTGAGT TGCTCGACCT CGCCTACTT GCGCTCTGT AGACACTTAG CGAAGTGTCTG

2801 CACGCTGATG AGCTTTACCG CAGCTGCCCT GCGGTTTTCG GTGATGACGG TGAAAACCTC TGACACATGC AGCTCCCGGA GACGGTCACA GCTTGTCTGT
GTCCGACTAC TCGAATGCG GTCGACGGAG CGGCCAAGC CACTACTGCC ACTTTTGGAG ACTGTGTACG TCGAGGGCCT CTGCCAGTGT CGAACAGACA

2901 AAGCGGATGC CGGGAGCAGA CAAGCCCGTC AGGCGGCTG AGCGGTGTT GCGGGGTGTC GGGGCGCAG CATGACCCAG TCACGTAGCG ATAGCGGAGT
TTCCGCTACG GCGCTCGTCT GTTCGGGCG TCCCGCGCAG TCCGCCACAA CCGCCGCTCG GTCCTGGTGC AGTGCACTCG TATCGCCTCA

3001 GTATACTGCG TTAACATATGC GGCATCAGAG CAGATTGTAC TGAGAGTGA CCATATGCGG TGTGAATATC CGCACAGATG CGTAAGGAGA AAATACCGCA
CATATGACCG AATTGATACG CCGTAGTCTC GTCTAACATG ACTCTCACGT GGTATACGCC ACACCTTTATG GCGTGTCTAC GCATTCTCT TTTATGGCGT

3101 TCAGGGCGTC TTCCGCTTCC TCGCTCACTG ACTCGCTGCG CTCGGTCTGTT CCGGTGCGG GAGCGGTATC AGCTCACTCA AAGCGGTAA TACGGTTATC
AGTCCGCGAG AAGCGNAGG AGCGAGTGAC TGAGCGACGC GAGCCAGCAA GCCGACGCG CTCGCCATAG TCGAGTGAGT TTCCGCCATT ATGCCAATAG

3201 CACAGAATCA GGGGATAACG CAGGAAAGAA CATGTGAGCA AAGGGCCAG AAGCCGTAA GAACCGGCTG TGCTGGCGTT TTTCCATAGG
GTGTCTTAGT CCGCTATTGC GTCTTTCTT GTACACTCGT TTTCCGGTCT TTTCCGGTCT TTTCCGGTCT TTTCCGGTCT TTTCCGGTCT

3301 CTCGCGCCCG CTGACGAGCA TCACAAAAAT CGACGCTCAA GTGCTGAGT CAGTCTCCAC CGCTTTGGG TGTCTGATA TTTCTATGGT CCGCAAAGGG GGCCTTCTGA
GAGGCGGGG GACTGCTCGT AGTGTCTTAA GCTGCGAGT GCTGCGAGT CAGTCTCCAC CGCTTTGGG TGTCTGATA TTTCTATGGT CCGCAAAGGG GGCCTTCTGA

3401 CCTCTGTCG CTCTCTGTT CCGACCTGTC CGCTTACCG ATACCTGTC ATACCTGTC GCTTTCTCC CTTCCGGGAG CGTGCGCTT TCTCATAGCT CACGCTGTAG
GGGAGCACGC GAGAGGACNA GGTGGGACG GCGAATGGCC TATGGACAGG CGGAAAGAG GAGCCCTTC GCACCGGAA AGAGTATCGA GTGCGACATC

3501 GTATCTCAGT TCGGTGTAGG TCGTTCGCTC CAGCTGGGCG GTTCGACCG GTTCGACCG GTTCGACCG GTTCGACCG GTTCGACCG GTTCGACCG GTTCGACCG
CATAGAGTCA AGCACATCC AGCACATCC AGCACATCC AGCACATCC AGCACATCC AGCACATCC AGCACATCC AGCACATCC AGCACATCC AGCACATCC

3601 GAGTCCAACC CCGTAAGACA CGACTTATCG CCACTGGCAG CAGCCACTGG TAACAGGATT AGCAGAGCGA GGTATGTAGG CCGTGCTACA GAGTTCTTGA
CTCAGGTTGG GCCATTCTGT GCTGAATAGC GGTGACCGTC GTGCTGAC ATTGTCTTAA TCGTCTCGCT CCATACATCC GCCACGATGT CTCGAAGAACT

3701 AGTGTGGGCC TAACTACGGC TACACTAGAA GGACAGTATT TGGTATCTGC GCTCTGCTGA AGCCAGTTAC AGCCAGTTAG AGAGTTGGTA GCTCTTGATC
TCACACCCGG ATTGATGCCG ATGTGATCTT CCTGTATATA ACCATAGACG CGAGACGACT TCGGTCAATG GAAGCCTTTT TCTCAACCAT CGAGAAGTAC

FIG. 3C

3801 CGGCANACAA ACCACCGCTG GTAGCGGTGG TTTTNTTGTG TGCAGCAGC AGATTACGGC CAGAAAAAAGG GATCTCTCAG GGATCTCCTT GATCTTTTCT
GCCGTTTGT TGGTGGCGAC CATGCCACCC AAAAAACAA ACSTTCGTG TCTATTCGCG GTCTTTTTT CCTAGAGTTC TTCTAGGAAA CTAGAAAAA
3901 ACGGGTCTG ACGTCACTG GAACGAAAAAC TCACGTTAAG GGAATTTGGT CATGAGATTA TCRAAAAGGA TCTTCACCTA GATCTTTTAA AATTAATAAT
TGCCCCAGAC TGGGAGTCAC CTTGCTTTTG AGTGAATTC AGTGAATTC CCAAAACCA GTACTCTAAT AGTTTTTCT AGAAGTGGAT CTAGGAAAAAT TTAATTTTAA
4001 GAAATTTTAA ATCAATCTAA AGTATATATG AGTAACCTTG GTCTGACAGT TACCAATGCT TAATCAGTGA GGCACCTATC TCACCGATCT GTCTATTTCT
CTTCAAAAT TAGTTAGATT TCATATATAC TCATTTGAAC CAGACTGTCA ATGTTTACGA ATTAGTCACT CCGTGGATAG AGTCCTAGA CAGATAAAGC
4101 TTCATCCATA GTTGCCCTGAC TCCCGCTGCT GTAGATAACT ACATATTTGA TGCTATGCCC TCCCGAATGG TAGACCGGG TCACGACGTT ACTATGGCGC TCTGGGTGG
AAGTAGGTAT CAACGGACTG AGGGCAGCA CATCTATTGA TGCTATGCCC TCCCGAATGG TAGACCGGG TCACGACGTT ACTATGGCGC TCTGGGTGG
4201 TCACCGGCTC CAGATTTATC AGCAATAAAC CAGCCAGCCG GAAGGCCGA GCGCAGAGT GGTCTCTGCA CTTTATCCGC CTCCATCCAG TCTATTAT
AGTGGCCGAG GTCTAAATAG TCGTTATTG GTCGGTGGC CTTCCCGCT CCGCTCTTCA CCAGGACGTT GAAATAGGCG GAGGTAGTCT AGATAAATTA
4301 GTTGCCGGGA AGCTAGAGTA AGTAGTTGCG CAGTTAATAG TTTGCGCAAC GTTGTGCGA TTGCTGCGAG CATCGTGGTG TCACGCTCGT CGTTTGGTAT
CAACGGCCCT TCGATCTCAT TCATCAAGCG GTCAATTATC AARCGCGTTG CAACAACGGT AACGACGTCC GTAGCACAC AGTGGGAGA GCRAACCAT
4401 GGTCTCATTC AGCTCCGCTT CCCAACGATC AAGCGAGTT ACATGATCCC CCATGTTGTG CAAAAAAAGCG GTTAGTCTCT TCGGTCTCTC GATCGTTGTC
CCGAAGTAAG TCGAGGCCAA GGGTTGCTAG TTTCCGCTCAA TGTACTAGGG GGTACAACAC GTTTTTTTCG CAATCGAGGA AGCCAGGAGG CTAGCAACAG
4501 AGAAGTAAGT TGGCCGCGCT GTTATCACTC ATGTTTATGG CAGCACTGCA TAATCTCTT ACTGTCATGC CATCCGTAAG ATGCTTTTCT GTGACTGGTG
TCTTCATTCA ACCGGCGTCA CAATAGTGAG TACCAATACC GTCGTGACGT ATTAAGAGAA TGACAGTACG GTAGSCATTC TACGAAAAA CACTGACCAC
4601 AGTACTCAAC CAAGTCATTG TGAGAAATAGT GTATGCGCGG ACCGAGTTGC TCTTGCCCGG CGTCAACACG GGTAATATACC GCGCCACATA GCAGAACTTT
TCATGAGTTG GTTCAGTAAG ACTCTTATCA CATACGCGCG TGGCTCAACG AGAACGGGCC GCAGTTGTGC CCTATTATGG CCGGTGTAT CGTCTTGAAA
4701 AAAAGTGCTC ATCATTGGAA AACGTTCTTC GGGGCGAAAA CTCTCAAGGA TCTTACCGCT GTTGAGATCC AGTTCGATGT AACCCACTCG TGCACCCCAAC
TTTTACAGAG TAGTAACCTT TTGCAAGAG CCCCCTTTT GAGAGTTCTT AGAATGGCGA CAACTCTAGG TCAAGCTACA TTGGGTGAGC ACGTGGGTG
4801 TGATCTTCAG CATCTTTTAC TTTTACACAGC GTTCTTGGGT GAGCAAAAAAC AGGAAGGCAA AATGCGGCAA AAAAGGGAAT AAGGGGAGCA CGGAATGTT
ACTAGAAGTC GTAGAAAAATG AAGTGCTCG CAAGACCCA CTCGTTTTTG TCTTCCGTT TTAACGCGCT TTTTCCCTTA TTCCCGCTGT GCCTTTACAA
4901 GAATACTCAT ACTCTTCTT TTTCAATATT ATTGAAGCAT TTATCAGGGT TATTGTCTCA ATAGTCCCA ATAACAGAGT ACTCGCTAT GTATNAACTT TTTTATTGT
CTTATGAGTA TGAGAAAGGA AAGTTATATA TAACCTTCGTA AATAGTCCCA ATAACAGAGT ACTCGCTAT GTATNAACTT TTTTATTGT
5001 AATAGGGGT CCGCCACAT TTTCCCGGAA AGTGCCACCT GACGTCTAAG AAACCATAT TATCATGACA TTAACCTATA AAAATAGGCG TATCAGGAG
TTATCCCAA GCGCGGTGTA AAGGGGCTT TCACGGTGA CTGAGATTC TTTGGTAATA ATAGTACTGT AATTGGATAT TTTTATCCG ATAGTCTCC
5101 CCCTTCTGTC TTCAA
GGGAAGCAG AAGTT

FIG. 3D

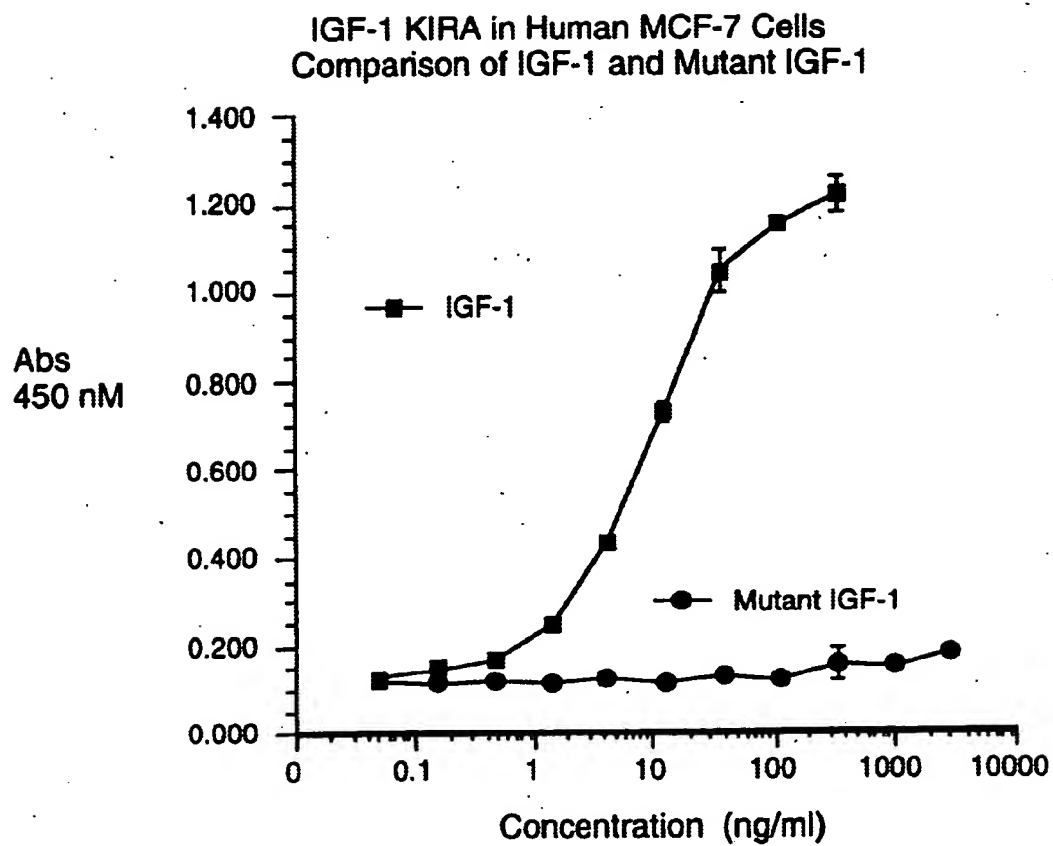


FIG. 4



IGF-1 (Leu²⁴ Ala³¹) is Inactive In Vitro

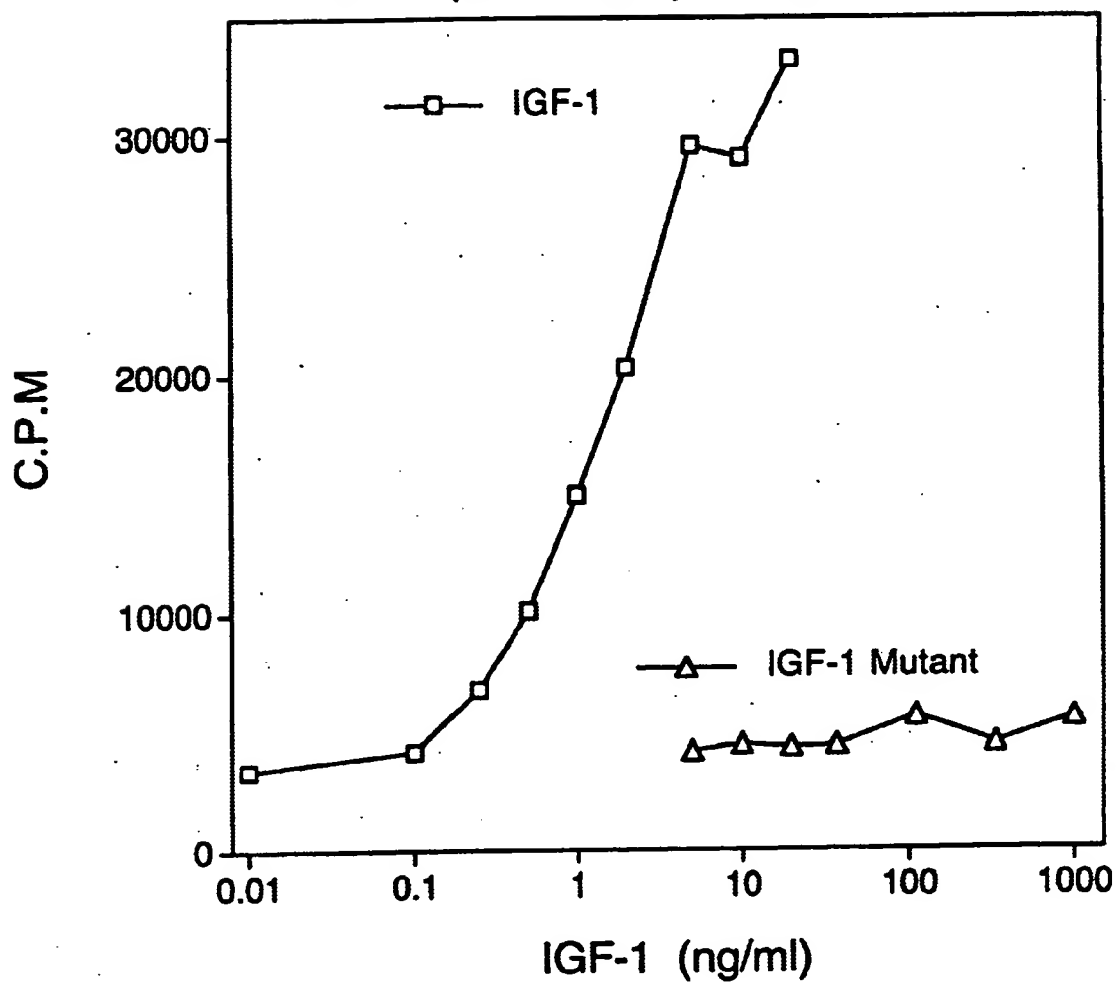


FIG. 5



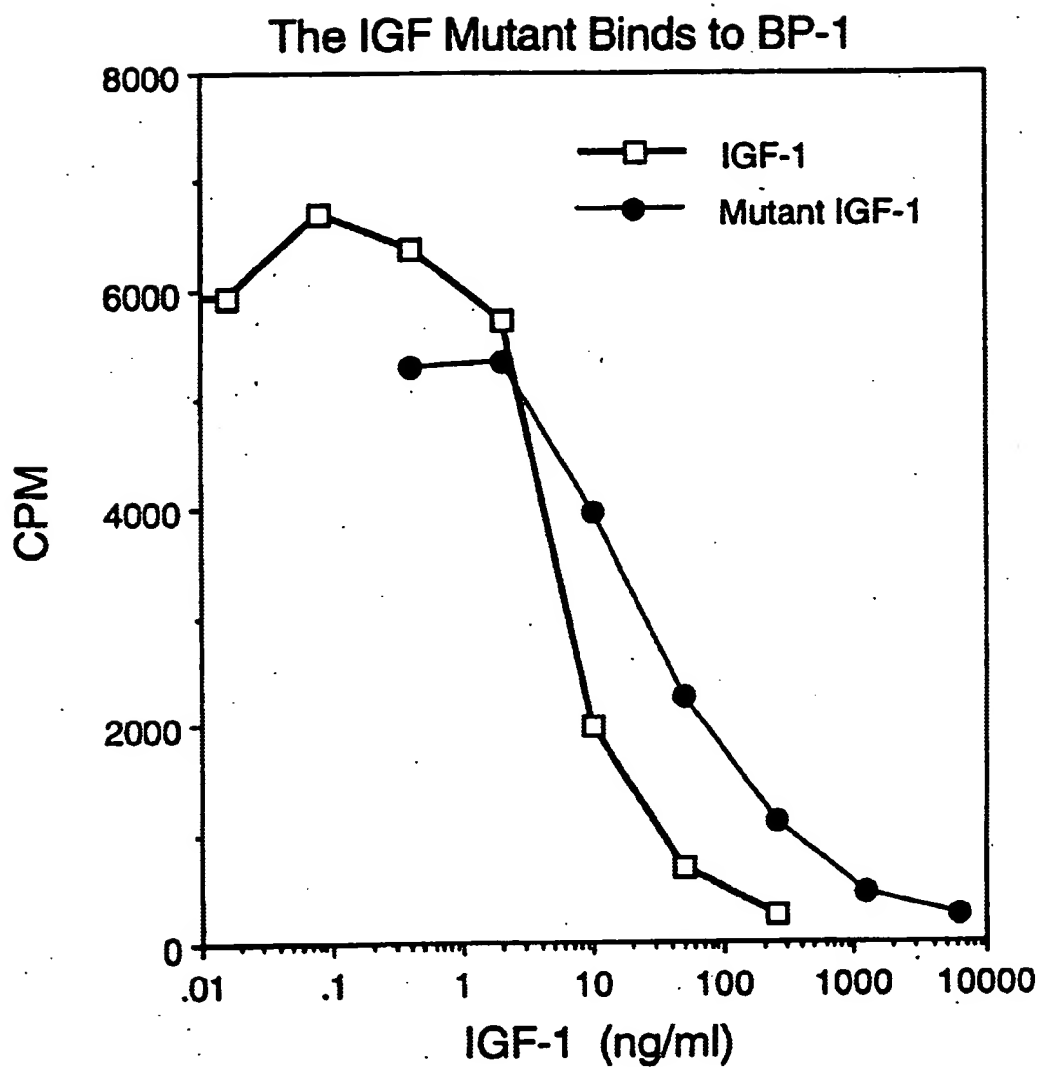


FIG. 6



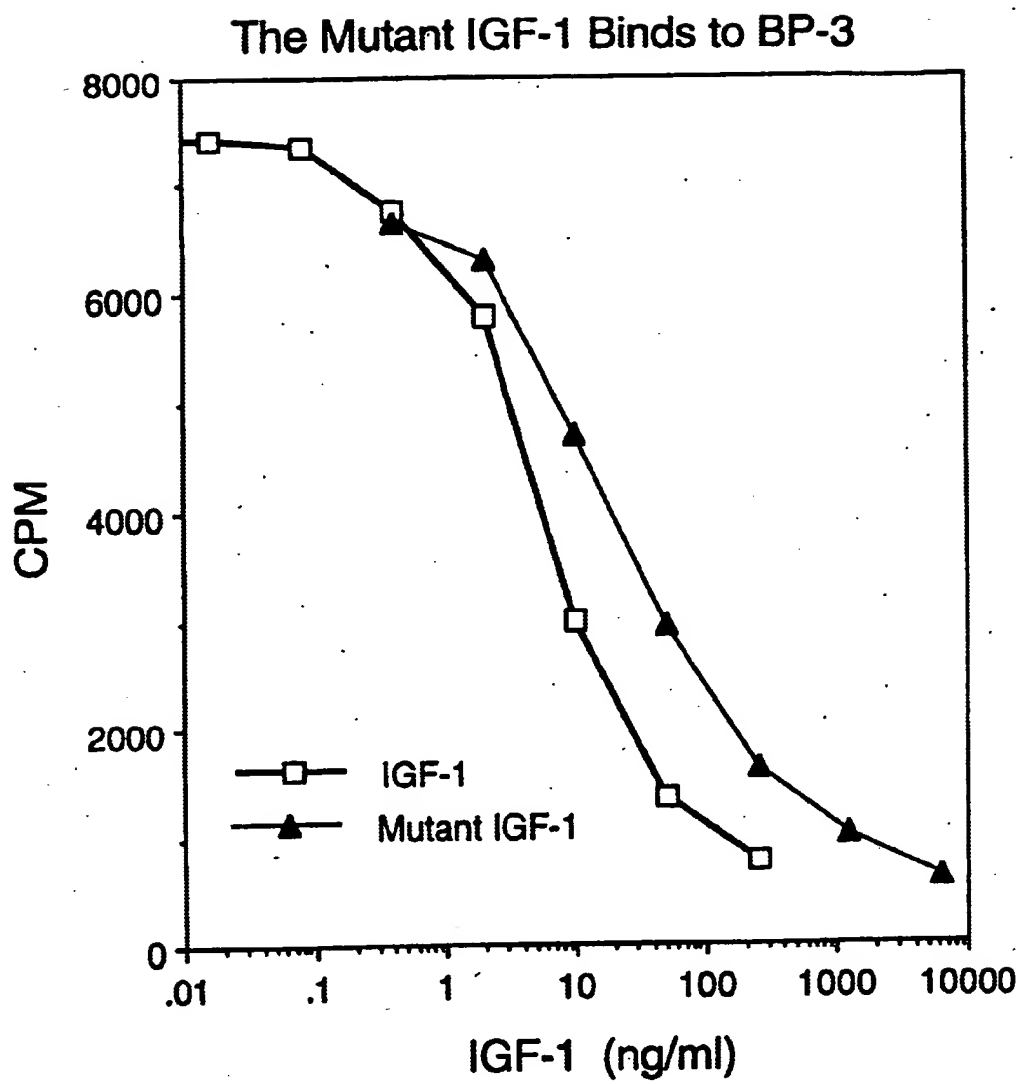


FIG. 7



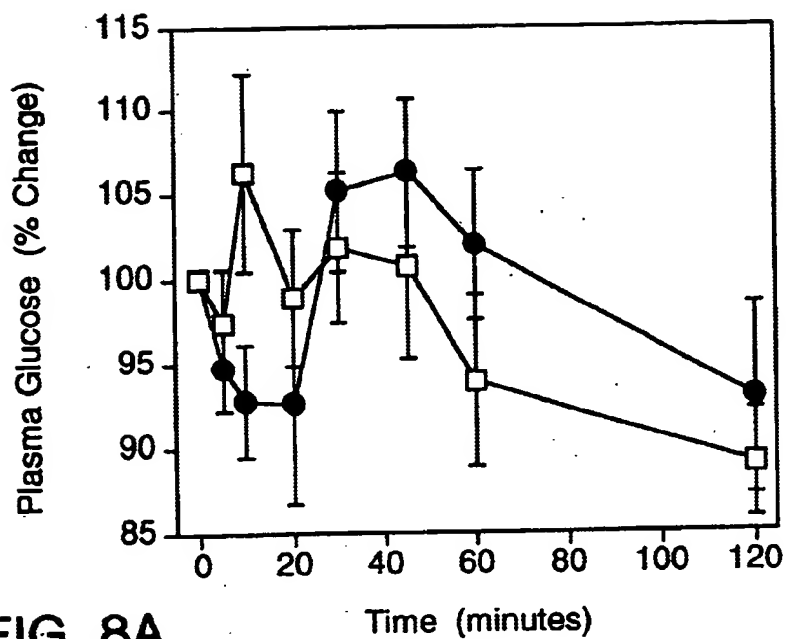


FIG. 8A

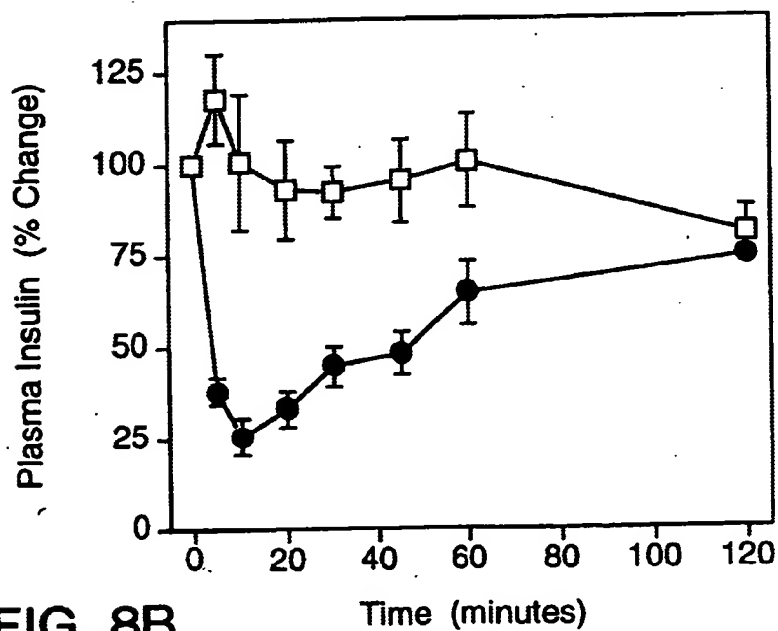


FIG. 8B

—□— Control —●— IGF-Mutant



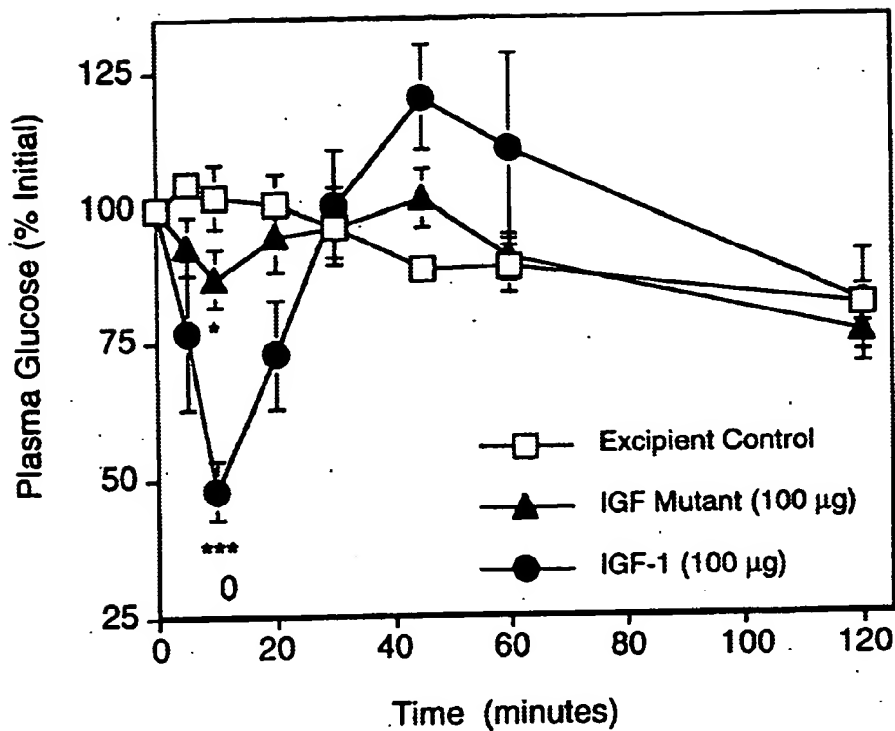


FIG. 9A

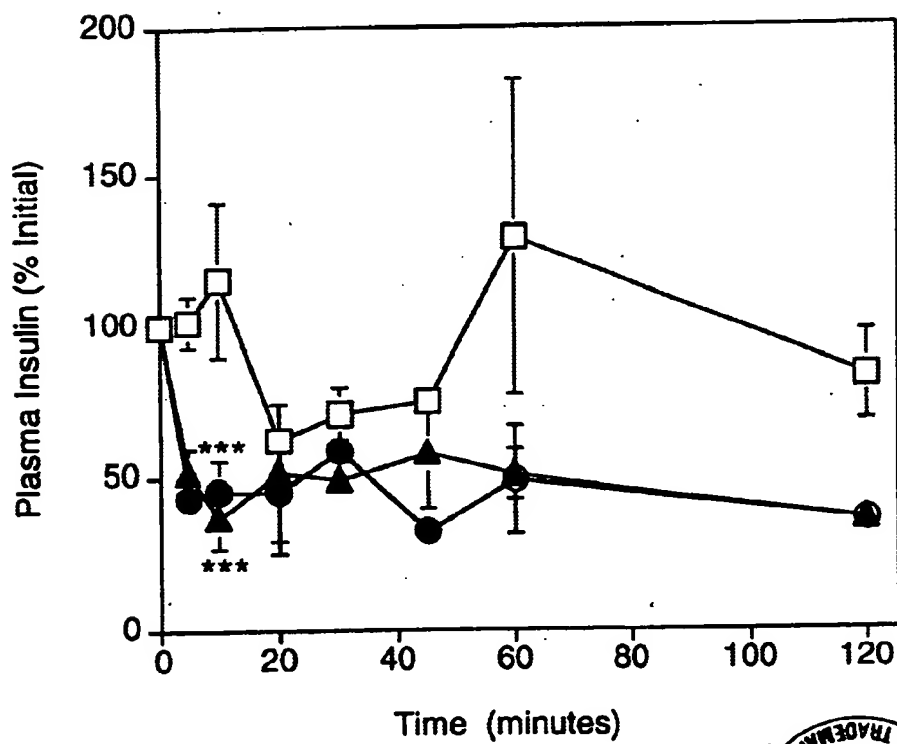


FIG. 9B



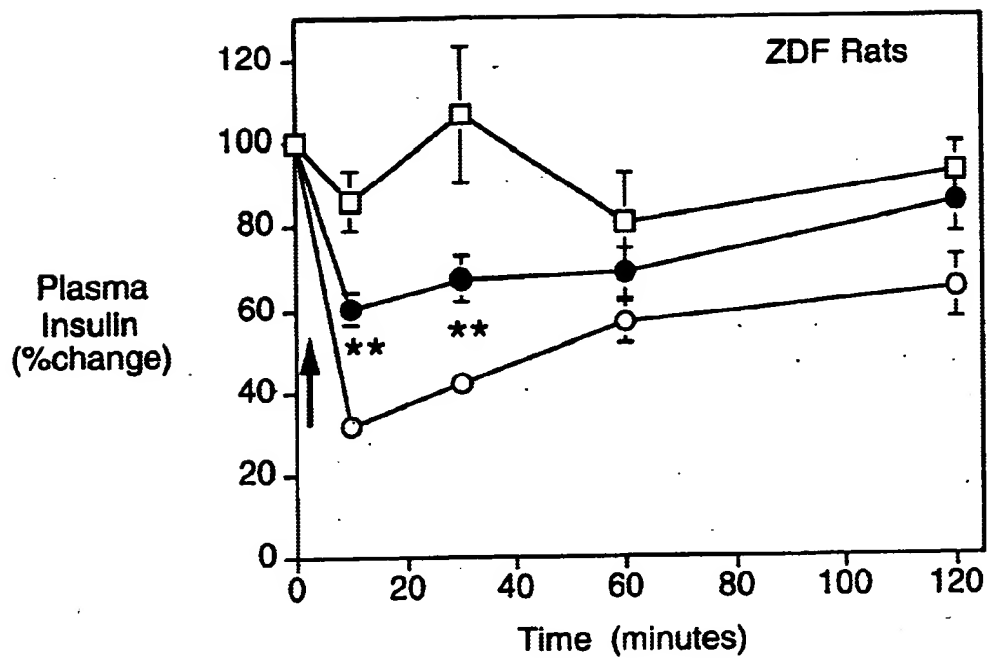


FIG. 10A

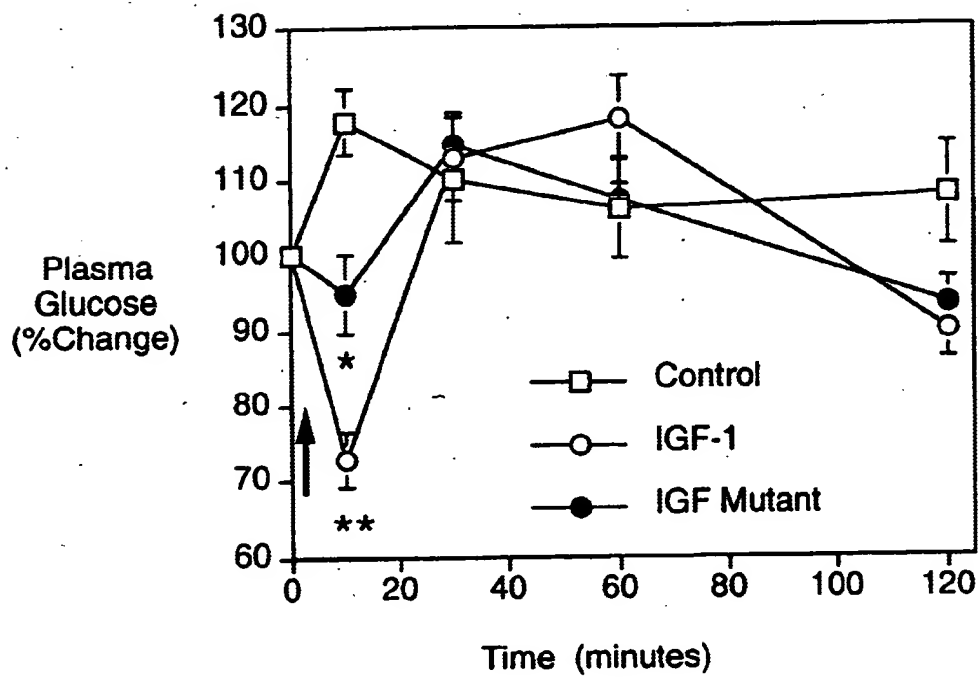
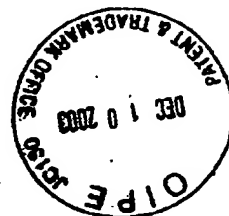


FIG. 10B



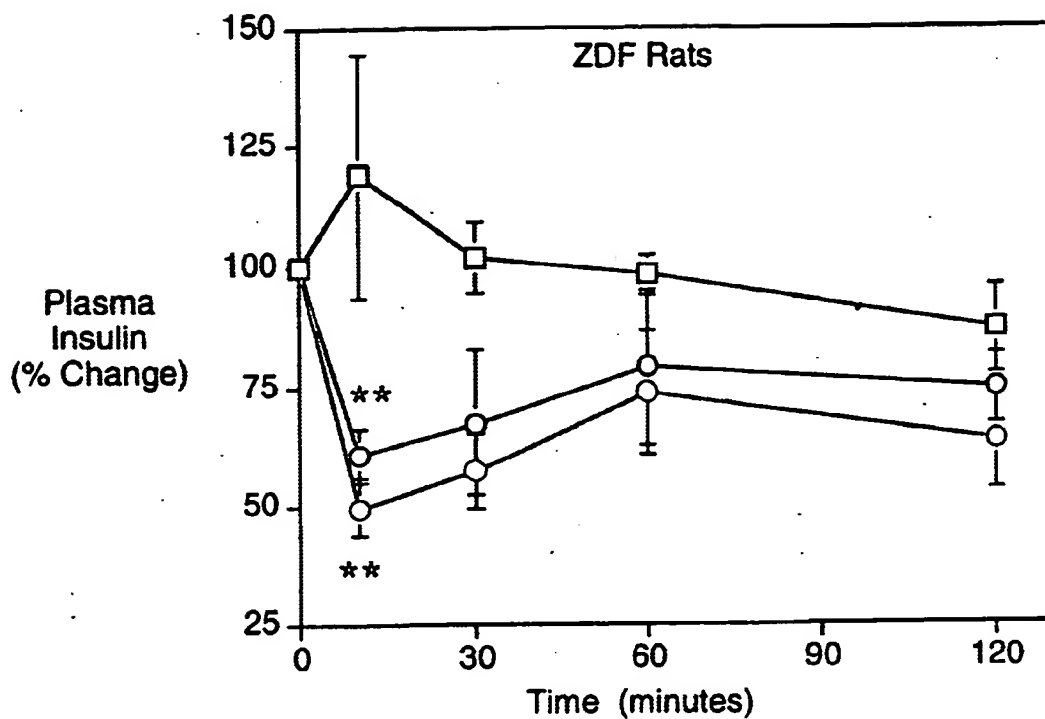


FIG. 11A

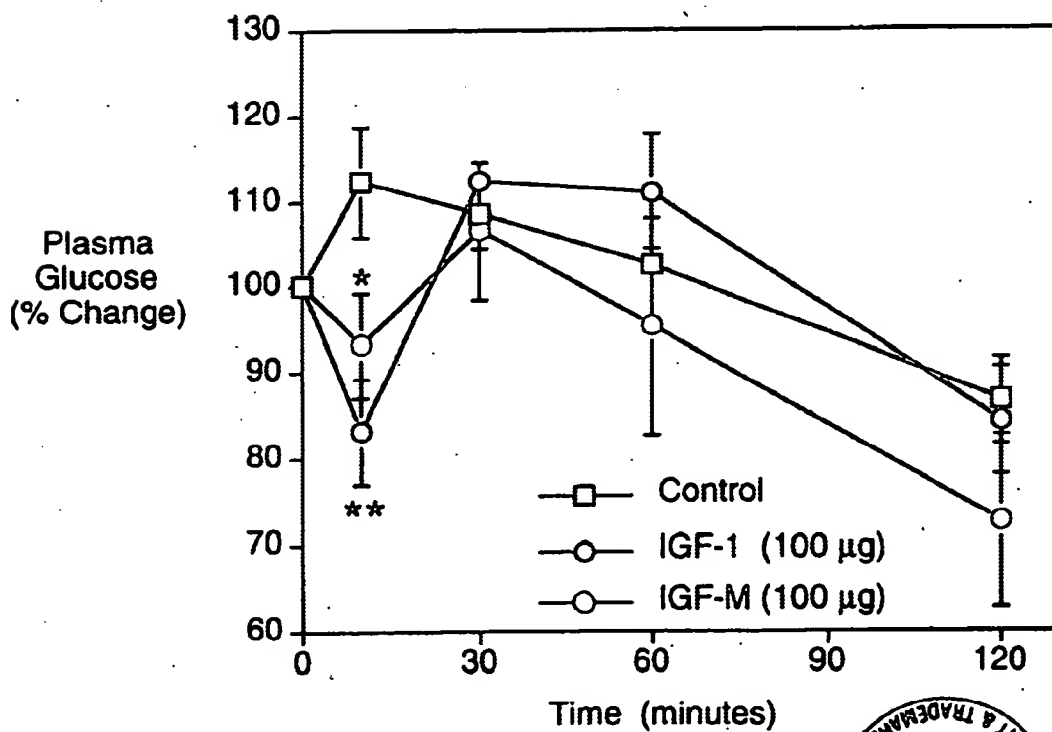


FIG. 11B



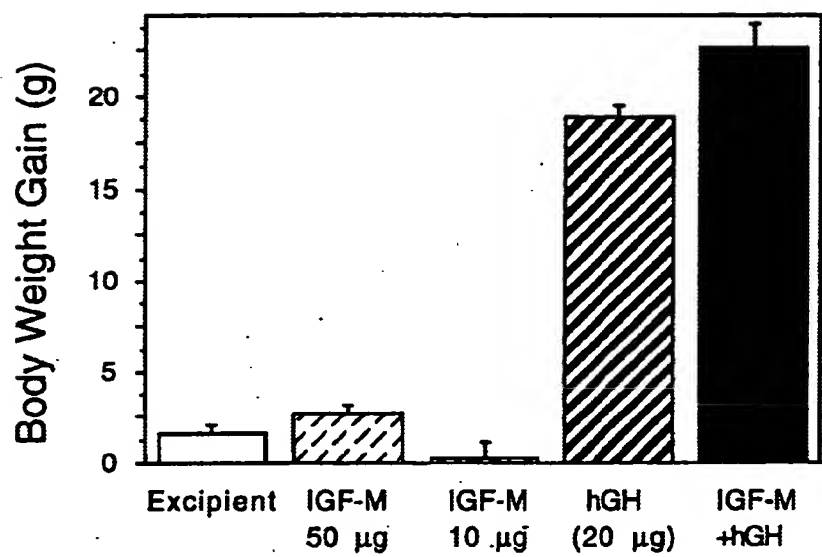


FIG. 12



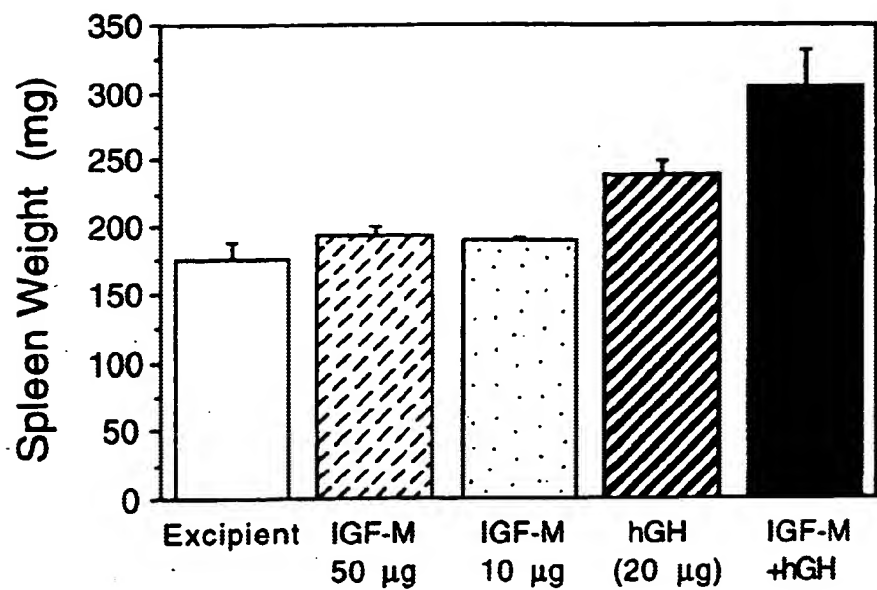


FIG. 13A

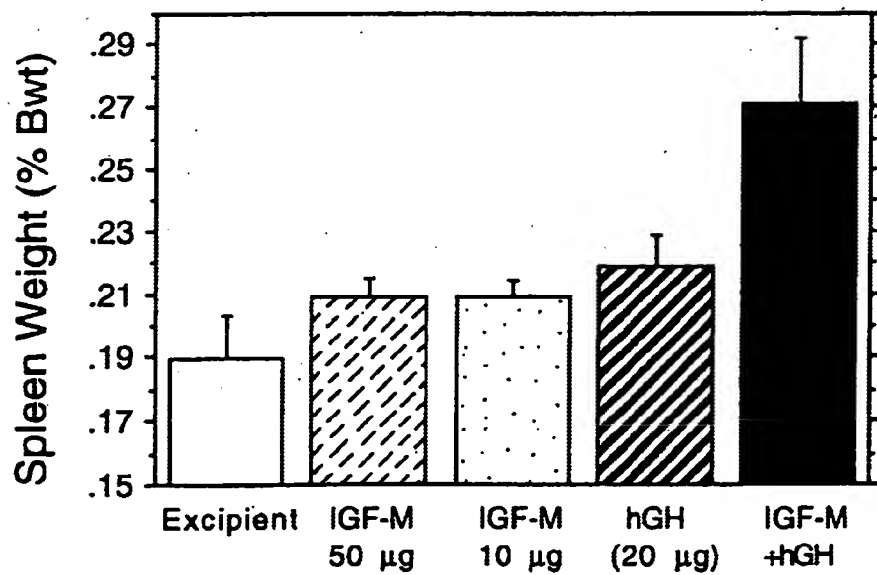


FIG. 13B



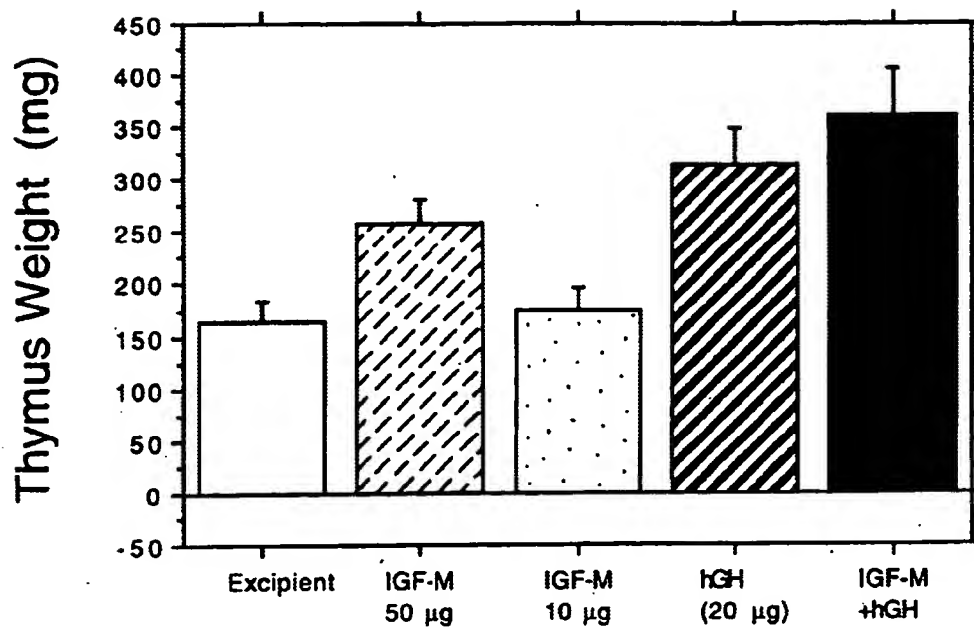


FIG. 14A

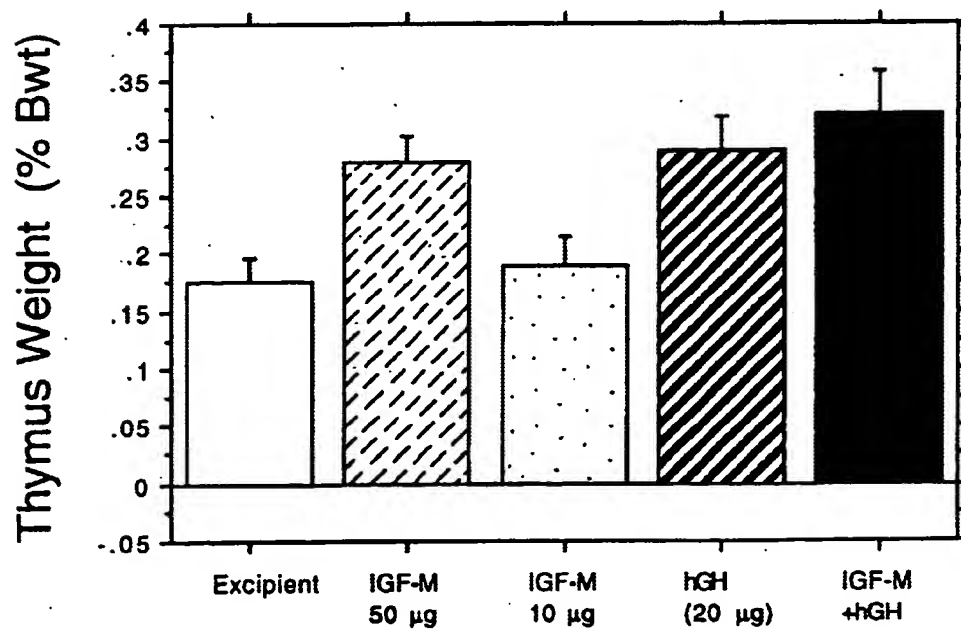


FIG. 14B



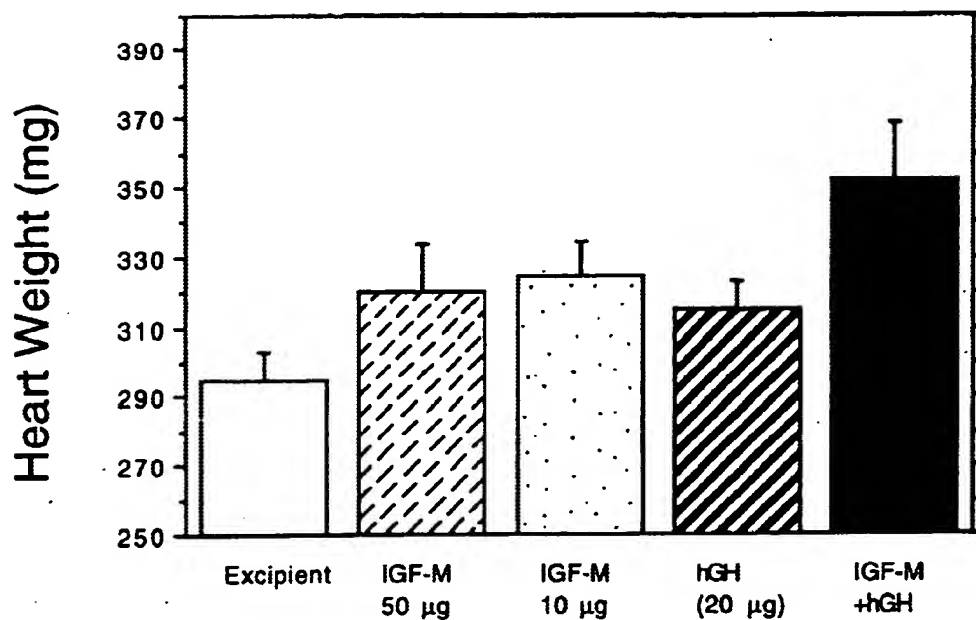


FIG. 15A

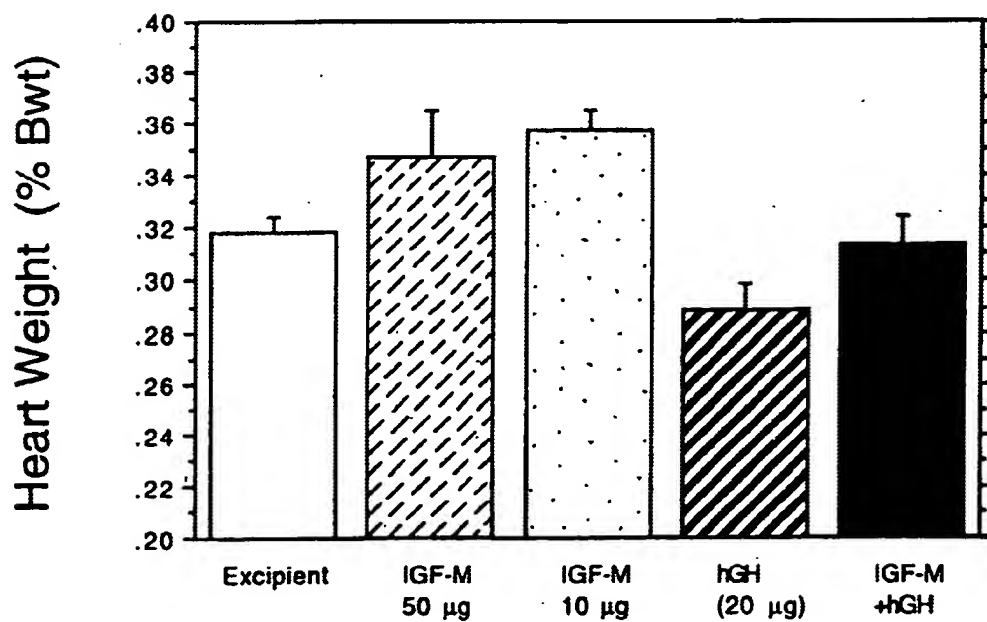


FIG. 15B



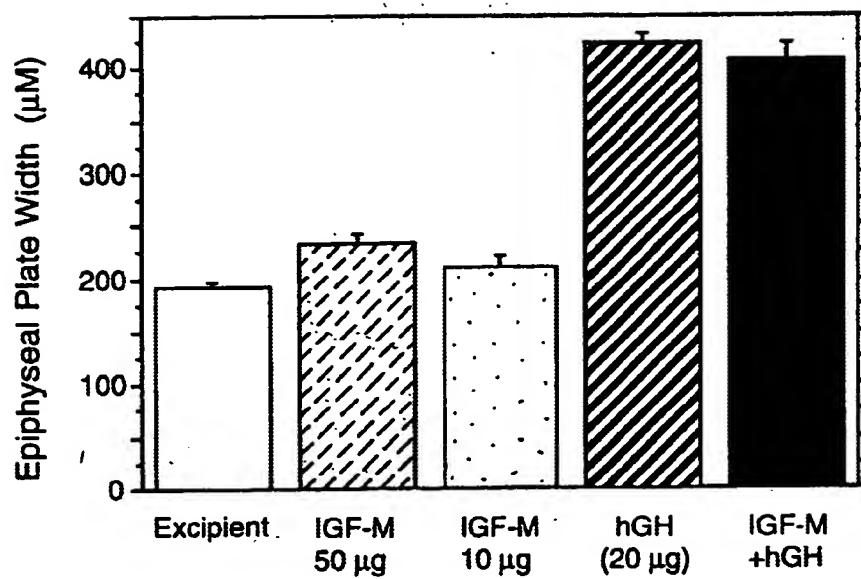


FIG. 16



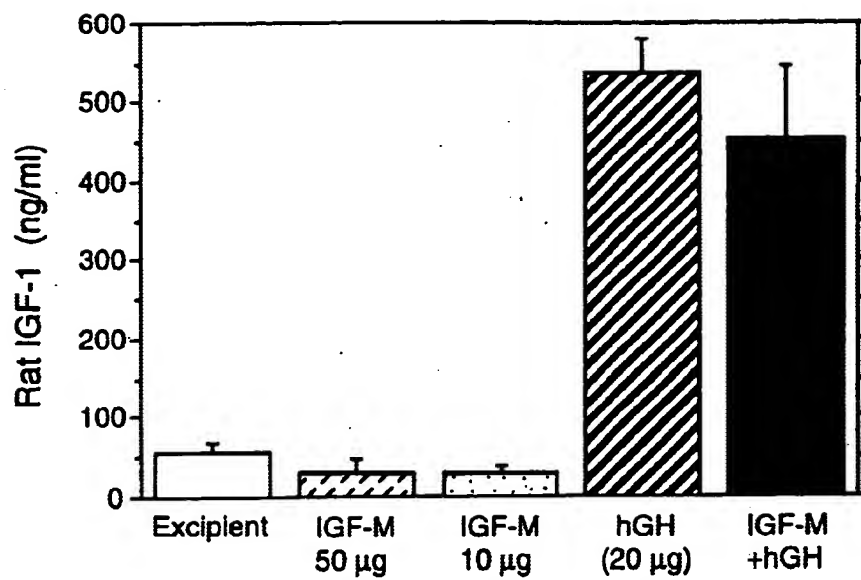


FIG. 17A

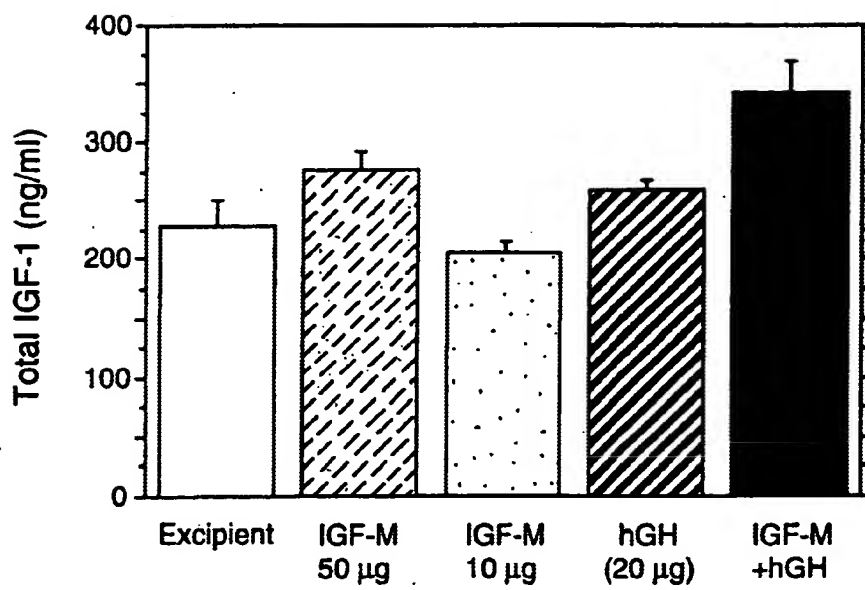


FIG. 17B



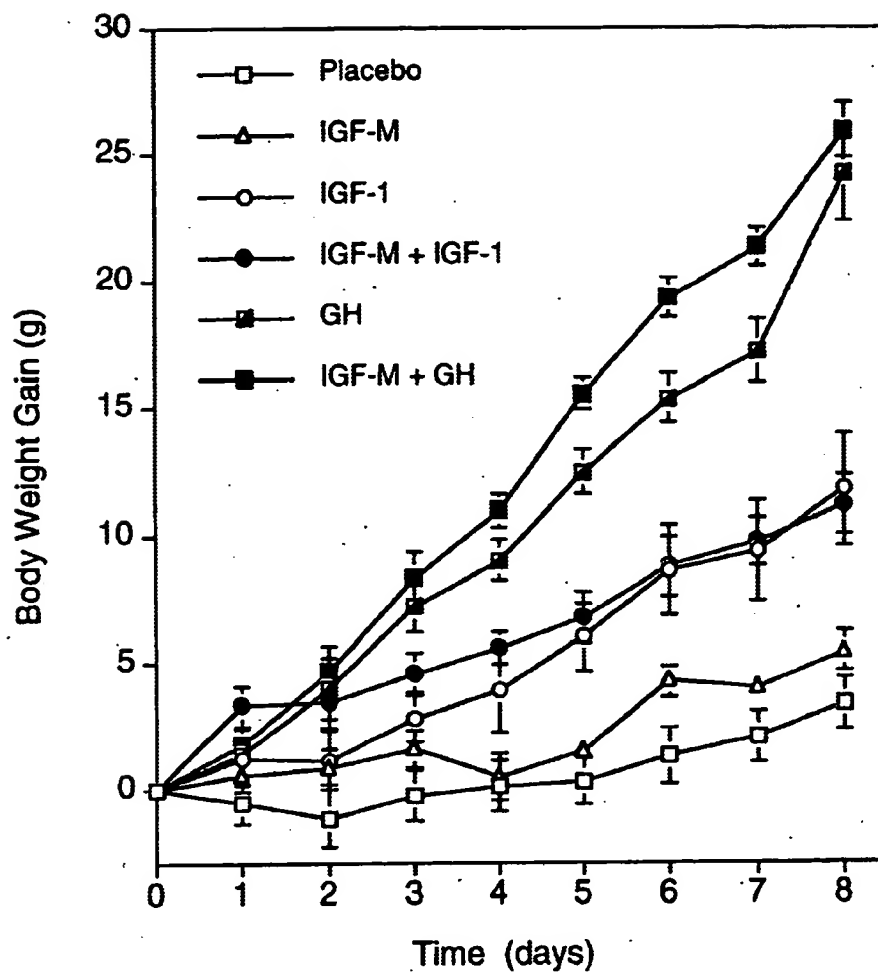


FIG. 18



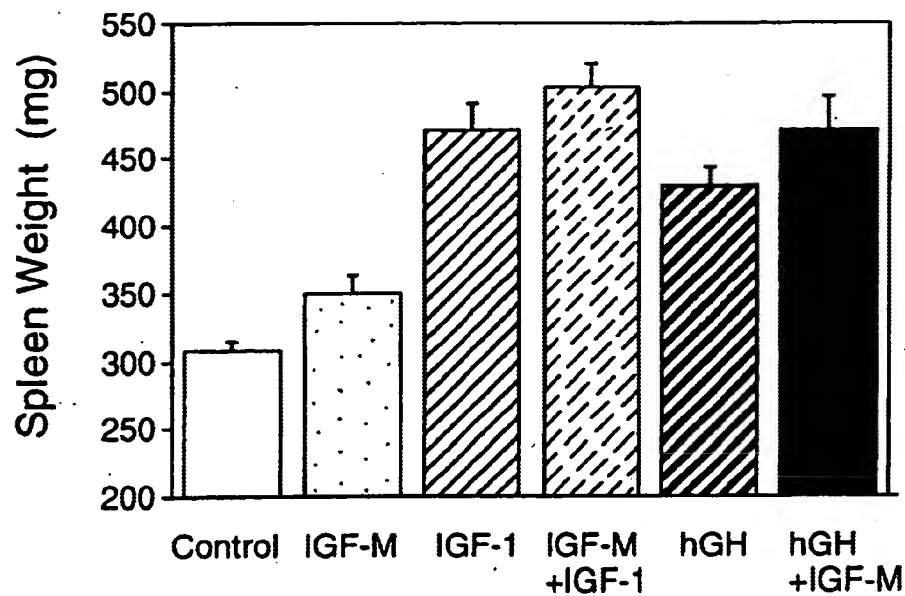


FIG. 19A

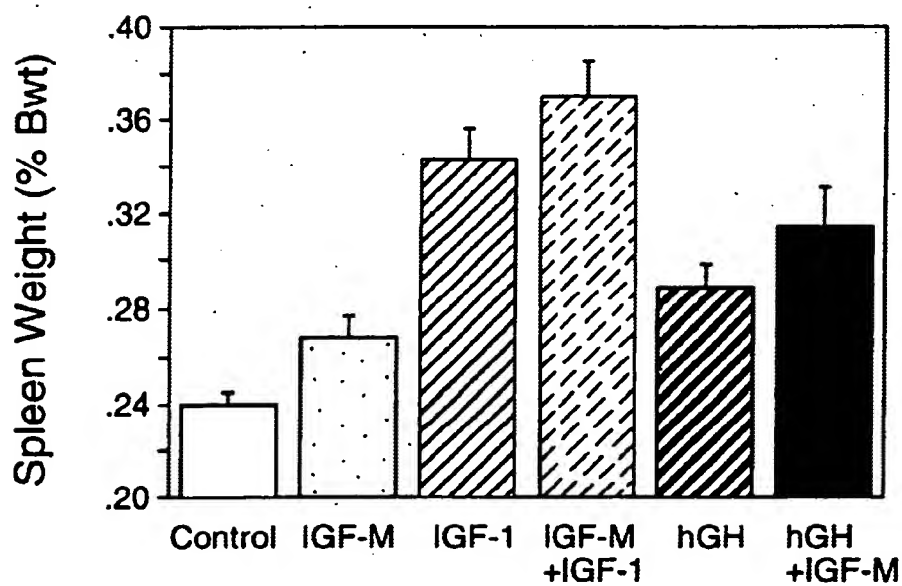


FIG. 19B



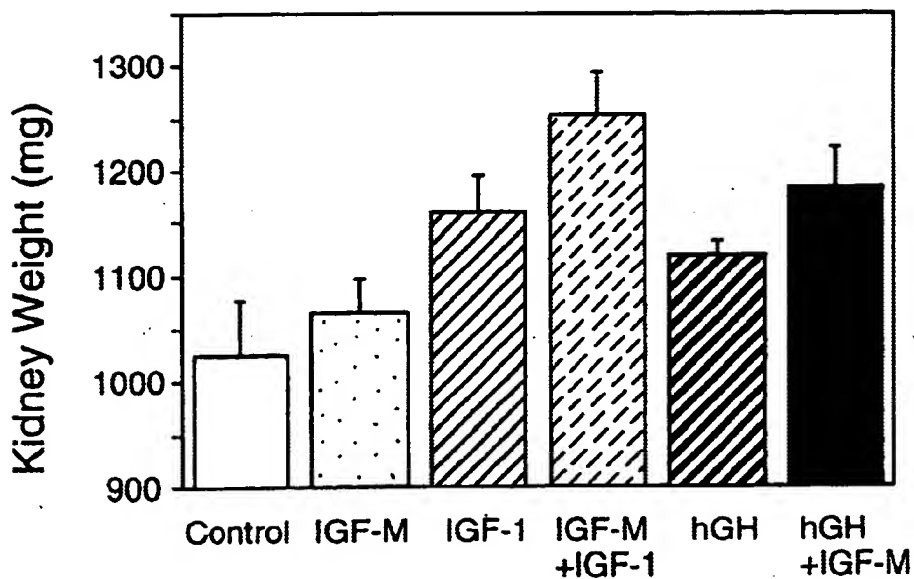


FIG. 20A

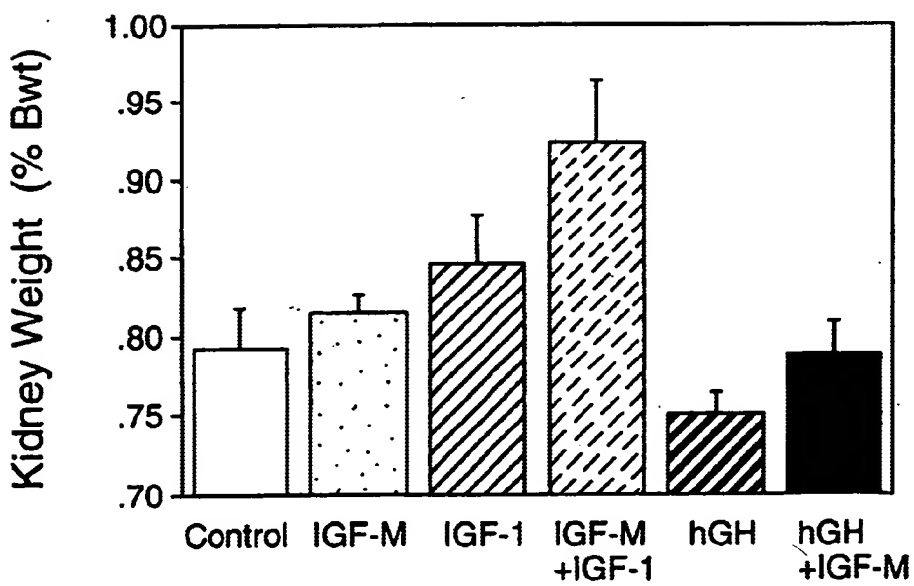


FIG. 20B



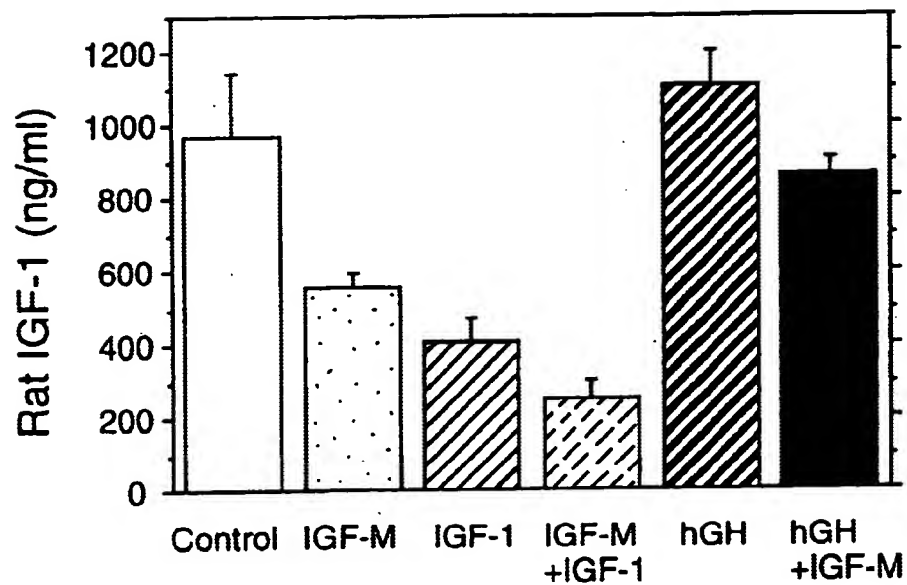


FIG. 21A

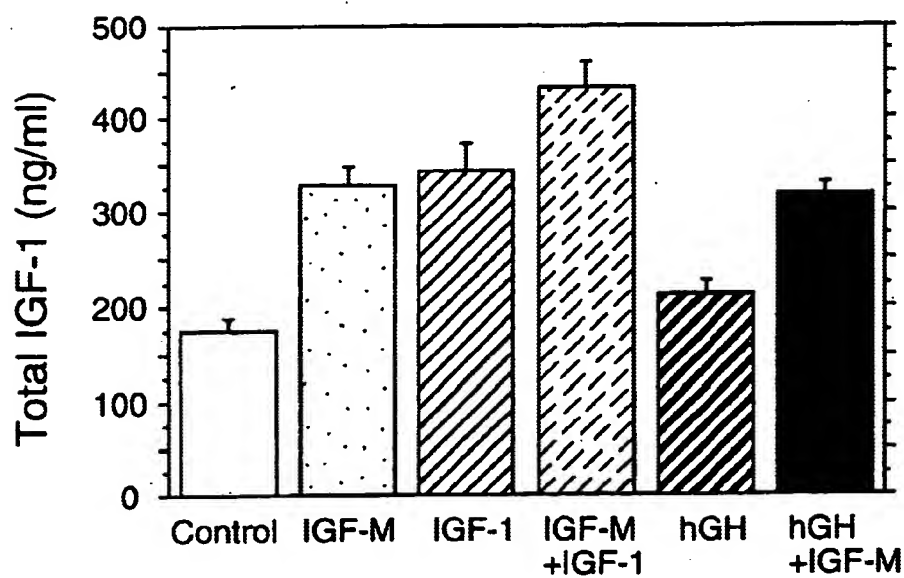


FIG. 21B



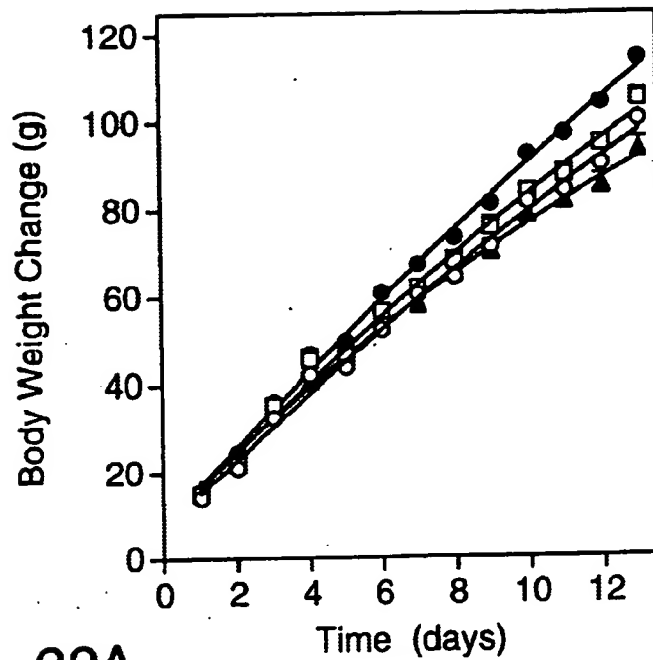


FIG. 22A

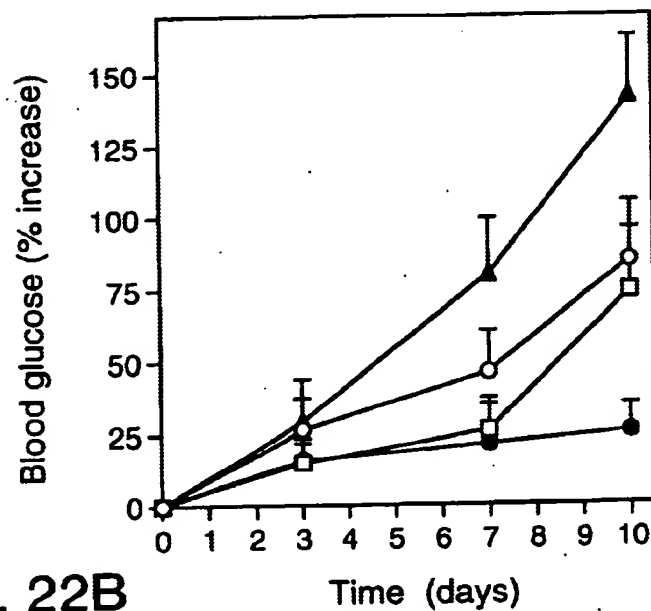
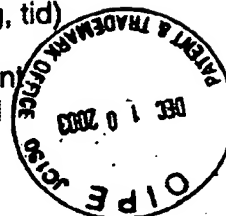


FIG. 22B

—●— IGF-1 (150 µg, tid) —□— IGF Mutant (150 µg, tid)
 —○— IGF Mutant (50 µg, tid) —▲— Excipient Control



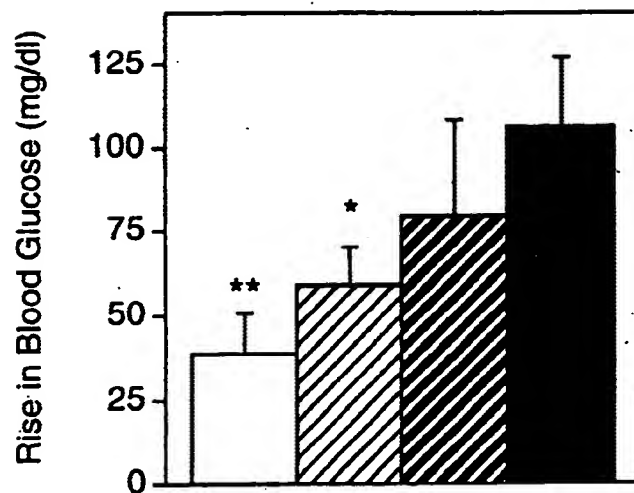


FIG. 23A

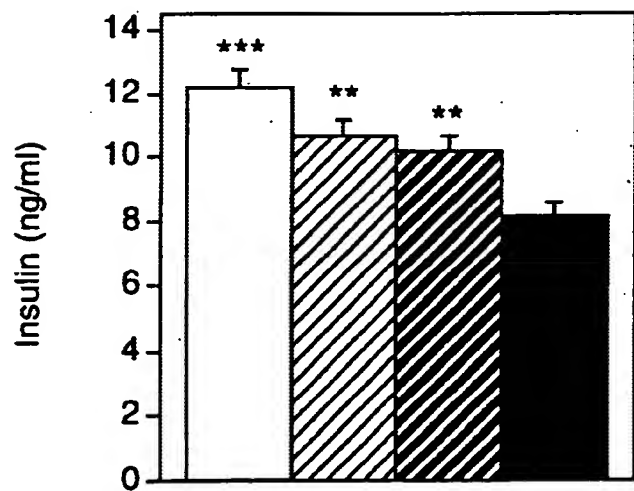


FIG. 23B

□ IGF-1 (150 µg, tid) ▨ IGF-Mutant (150 µg, tid)
 ▩ IGF-Mutant (50 µg, tid) ■ Control



plasmid t4.98

length: 5140 (circular)

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CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTCG TACTTTTTAG ACTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACGTGTG CCGAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTIACGA AGCGTTATAC CGCGTTTTAC TGGTGTGCG CAACCTAATA GTCCATCTCC

201 GGGCGCTGA CGAGGTAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGTGTGTC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCAACA GCTGTCAATA AGTTGTACAG GCGGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TTTGTAACTA GTACGGCAAGT
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CCGCTCTGAA TATCAGCGAA AAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAA AGGTTATCTA GAGGTTGAGG TGATTTTATG AAAAAAATA TCGCATTTCT TCTTGATCT ATGTTGCTTT TTTCTATTGC TACAAATGCC
AGTGCATTTT TCCCATAGAT CTCCAACTCC ACTAAATAC TTTTCTTAT AGCGTAAAGA AGAACGTAGA TACAAGCAAA AAAGATACG ATGTTTACGG

501 TATGCACTG GTACCGCCAT GGCTGATCCG AACCGTTTCC GCGTAAAGA TCTGGCAGGT TCACCAGGTG GAGGATCCGG AGGAGGCGCC GAGGTTGACG
ATACGTAGAC CATGCGGTA CCGACTAGC TTGGCAAGG CGCATTTCT AGACCGTCCA AGTGTCCAC CTCCTAGGCC CTCCTAGGCC CTCCCACTGC

1 1 SerG lythrAlaMe tAlaaspPro AsnArgphea rgGlyLysas pLeuAlaGly SerProGlyG lyGlyGlyAla GluglyAspasp

601 ATCCCGCAA AGCGCCTTT AACTCCCTGC AGCCTCAGC GACCGAATAT ATCGGTTATG CGTGGGCGAT GGTGTTGTC ATTGTCGGCG CAACATATCGG
TAGGGGTTT TCGCGGAAA TTGAGGGAGC TTGGAGTTCG CTGGCTTATA TAGCCCAATAC GCACCCGCTA CCAACAACAG TAACAGCGCG GTTGATAGCC

33 ProAlaLy sAlaAlaPhe AsnSerLeug InAlaSerAl aThrGluTyr IleGlyTyra laTrpAlaMe tValValVal IleValGlyA laThrIleGly

701 TATCAAGCTG TTTAAGAAAT TCACCTCGAA AGCAAGCTGA TAAACCGATA CAATTAAAGG CTCCTTTTGG AGCCTTTTGT TTTGGAGATT TTCAACGTGA
ATAGTTCGAC AAATTTCTTA AGTGGAGCTT TCGTTCGACT ATTTGGCTAT GTTAATTTCC GAGGAAAAA TCGGAAAAA AAACCTCTAA AAGTTGCACT

66 IleLysLeu PheLysLysP heThrSerLy salaSer

801 AAAAATTATT ATTGCAATT CCTTTAGTTG TTCTTTCTA TTCTCACTCC GCTGAACTG TTGAAAGTTG TTTAGCAAAA CCCCATACAG AAAATTCAAT
TTTTTAATAA TAAGCGTAA GGAATCAAC AAGGAAAGAT AAGAGTGAGG CGACTTTGAC AACTTTCAC AAATCGTTTT GGGGTATGTC TTTTAAGTAA

901 TACTAACGTC TGGAAAGACG ACAAACTTT AGATCGTTAC GCTAACTATG AGGTTGTCT GTGGAATGCT ACAGGCGTTG TAGTTTGTAC TGTGACGAA
ATGATTGCAG ACCTTTCTGC TGTTTTAAA TCTAGCAATG CGATTGTATC TCCCAACAGA CACTTACGA TGTCCGCMAC ATCAAAACATG ACCACTGCTT

1001 ACTCAGTGC TAGCTAGCT GCGGTTGGCT CTGTTCCGG TGATTTGAT TATGAAAAGA TGGCAAAACG TAATAAGGGG GCTATGACCG AAATGCCGA
TGAGTCACAG ATCGATCTCA CGGCCACCGA GACCAAGGCC ACTAAAACTA ATACTTTCT ACCGTTTGG ATTATTCCCC CGATACGGC TTTTACGGCT
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FIG. 24A



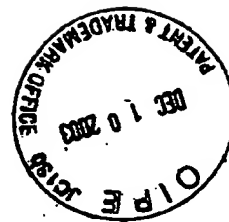
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ACTTTTGCGC GATGTCAGAC TCGGATTTCG GTTTGAACTA AGACAGCGAT GACTAATGCC ACAGCATAG CTACCAAAGT AACCACTGCA AAGGCCGMA
1201 GCTAATGGTA ATGGTGCTAC TGGTGATTTT GCTGGCTCTA ATTCCCAAT GGCTCAAGTC GGTGACGGTG ATAATTCCACC TTTAATGAAT AATTTCCGTC
CGATTACCAT TACCACGATG ACCACTAAAA CGACCGAGAT TAAGGGTTTA CCGAGTTTCA CCACTGCCAC TATTAAGTGG AAATTACTTA TTAAGGCCAG
1301 AATATTTTACC TTCCCTCCCT CAATCGGTTG AATGTGCGCC TTTTGTCTTT AGCGTGGTA AACCATATGA ATTTTCTATT GATTGTGACA AAATAAACCTT
TTATRAATGG AAGGGAGGGA GTTAGCCAAAC TTACAGCGGG AAAACAGAAA TCGCGACCAT TTGGTATACT TAAAGATATA TTTATTTGAA
1401 ATTCGGTGGT GTCTTTGGCT TTCTTTTATA TGTGTCACCT TTTATGTATG TATTTTCTAC GTTTGCTAAC ATACTGCGTA ATNAGGAGTC TTAATCATGC
TAAGGCACCA CAGAACGCA AAGAAAATAT ACACGCTGG AATACATAC TTTTATGATG AATAAGATG CAAACGATTG TATGACGCAT TATTCCTCAG AATTAGTACG
3201 ACTCAAAGGC GGTAAATACGG TTATCCACAG AATCAGGGGA TAACGCAGGA AAGAACATGT GAGCAAAAG CCAGCAAAG GCCAGGAACC GTAAAAAGGC
TGAGTTTCCG CCATTATGCC AATAGTGTC TTAGTCCCT ATGCGTCTT TCTTTGTACA CTGTTTTCC GGTGTTTTTC CGGTCTCTGG CATTTTTCGG
3301 CGCGTTGCTG GCGTTTTTCC ATAGGCTCGG CCCCCTGAC GAGCATACA AAATCGACG CTCNAGTCAG AGGTGGCGAA ACCGACAGG ACTATAAAGA
GCGCAACGAC CGCAAAAAGG TATCCGAGGC GGGGGGACTG CTGCTAGTGT TTTTAGCTGC GAGTTCAGTC TCCACCGCTT TGGGCTGTCC TGATATTTCT
3401 TACCAGGCGT TTCCOCTGG AAGTCCCTC GTGCGTCTC CTGTTCCGAC CCGTCCGCTT ACCGGATACC TGTCGCTCTG GGAAGCGTGG
ATGGTCCGCA AAGGGGACC TTCCAGGGAG CACGCGAGAG GACAAGGCTG GGACGGCGAA TGGCTATAG ACAGCGGAA AGAGGGAAGC CCTTCGCACC
3501 CGCTTTCTCA TAGTCAAGC TGATAGTATC TCAGTTGGT GTAGTCTGTT CGTCCCAAGC TGGGCTGTGT GCACGAAACC CCGTTCAGC CCGACCGCTG
GCGAAAGAGT ATCGAGTGG ACATCCATAG AGTCAAGCCA CATCCAGCAA CGAGGTTGG ACCCGACACA CGTCTTGGG GGGCAAGTCG GGCTGGCGAC
3601 CGCCTTATCC GGTAACTATC GTCTTGAGTC CAACCCGGTA AGACACGACT TATCGCCACT GGCAGCAGCC ACTGCTAACA GGATTAGCAG AGCGAGGTAT
GCGGAATAGG CCATTGATAG CAGAACTCAG GTTGGGCCAT TCTGTGCTGA ATAGCGGTGA CCGTCTGCTG TGACCATGT CCAATCTGTC TCGCTCCATA
3701 GTAGGCGGTG CTACAGAGTT CTTGAAGTGG TGGCCTAACT ACGGCTACAC TAGAAGGACA GTATTGGTA TCTGCGCTCT GCTGAAGCCA GTTACCTTGG
CATCCGCCAC GATGCTCAA GAACCTTACC ACCGGATTGA TGGCGATG TGCCGATG ATCTTCTCT CATAAACCAT AGACGCGAGA CGACTTCGT CAATGGAAGC
3801 GAAAAAGAGT TGGTAGTCT TGATCCGGCA AACAAACCAC CGTGGTAGC GGTGGTTTTT TGTGTTGCAA GCAGCAGATT ACGCGCAGAA AAAAAGGATC
CTTTTCTCA ACCATCGAGA ACTAGGCCGT TTGTTTGGTG GCGACCATCG CCACCAAAAA AACAAACGTT CGTCTGCTTA TCGCGCTCTT TTTTCTCTAG
3901 TCAAGAGAT CTTTGTATCT TTTTCTACGG GTCTGACGCT CAGTGGAAAG AAAACTCAG TTAAGGGATT TTGGTCAAGA GATTATCAA AAGGATCTTC
AGTTCTCTA GGAACCTAGA AAGATGCCC CAGACTGCGA GTCACTTGC TTTTGGTGG AATTCCTTA AACCACTACT CTAATAGTTT TTCTAGAGA
4001 ACCTAGATCC TTTTAATTA AAAATGAAGT TTTAATCAA TCTAAGTAT ATATGAGTAA ACTTGGTCTG ACAGTTACCA ATGCTTAATC AGTGAGGCAC
TGGATCTAGG AAAATTAAT TTTTACTTCA AATTTAGT TATACTCAT AGATTTCATA TATACTCAT TGAACACAGAC TGTCATATGT TACGAATTAG TCACTCCGCG

FIG. 24B



4101 CTATCTCAGC GATCTGTCTA TTTCTGTTTCAT CCATAGTTGC CTGACTCCCC GTCGTGTAGA TAACTACGAT ACGGGAGGGC TTACCAATCTG GCCCCAGTGC
 GATAGAGTCG CTAGACAGAT AAAGCAAGTA GGTATCAACG GACTGAGGG CAGCAATCT ATTGATGCTA TGCCCTCCCG AATGGTAGAC CGGGGTACAG
 4201 TGCAATGATA CCGCGAGACC CACGCTCACC GGCTCCAGAT TTATCAGCAA TAAACAGCC AGCGGAAGG GCCGAGCGCA GAAAGTGTCC TGCNACTTTA
 ACGTTACTAT GCGCTCTGG GTGCGAGTGG CCGAGGTCTA AATAGTCGTT ATTTGTCGG TCGGCTTCC CGGCTCGCGT CTTACACAGG ACGTTGAAAT
 4301 TCCGCTCCA TCCAGTCTAT TAATTGTTGC CCGGAAGCTA GAGTAAGTAG TTGCGCAGTT AATAGTTTGC GCAACGTTGT TGCCATTTGT GCAGGCATCG
 AGCGGAGGT AGGTACAGATA ATTAACAACG GCCCTTCGAT CTCATTTCATC AAGCGGTCAA TTATCAACG CGTTGCAACA ACGGTACGA CGTCCGTAGC
 4401 TGGTGTCAOG CTCGTGCTTT GGTATGGCTT CATTCAGCTC CGGTTCCCAA OGATCAGGC GAGTTACATG ATCCCCCATG TTGTGCAAAA AAGCGGTTAG
 ACCACAGTGC GAGCAGCAA CCATACCGAA GTAAAGTCGAG GCCAAGGTT GCTAGTTCCG CTCGAATGTAC TAGGGGTAC AACACGTTTT TCGCCNATC
 4501 CTCCTTCGGT CCTCCGATCG TTGTCAGAG TAAGTTGGCC GCAGTGTAT CACTCATGCT TATGGCAGCA CTGCATAATT CTCTTACTGT CATGCCATCC
 GAGGAAGCCA GGAGGCTAGC AACAGTCTTC ATTCAACCGG CGTCACAATA GTGAGTACCA ATACGTCGT GACGTATTA GAGAATGACA GTACGGTAGG
 4601 GTAAGATGCT TTTCTGTGAC TGGTGAGTAC TCAACCAAGT TCATCTGAGA ATAGTGTATG CCGCGACCGA GTTGCTCTTG CCCGGCGTCA ACACGGGATA
 CATCTACGA AAAGACACTG ACCACTCATG AGTTGGTTCA GTAGACTCT TATCACATAC GCCGCTGGCT CAACGAGAAC GGGCCGCGAGT TGTGCCCTAT
 4701 ATACCGCGCC ACATAGAGA ACTTTAAAAG TGCTCATCAT TGGAAAACGT TCTTCGGGGC GAAAACTCTC AAGGATCTTA CCGCTGTTGA GATCCAGTTC
 TATGGCGCGG TGTATCTGCT TGAATTTTC ACGAGTAGTA ACCTTTTCGA AGAAGCCCCG CTTTGTAGAG TTCTAGAAAT GCGGACAACT CTAGGTCAAG
 4801 GATCTAACCC ACTCGTGCAC CCAACTGATC TTCAGCATCT TTTACTTTCA CCAGCGTTTC TGGGTGAGCA AAAACAGGAA GGCAAAATGC CGCAAAAAAG
 CTACATTTGG TGAGCACGTG GGTGACTAG AAGTCGTAGA AAATGAAAGT GGTGCAAG ACCCACTCGT TTTTGTCCCT TTTTGTACG GCGTTTTTTC
 4901 GGAATAGGG CGACACGGAA ATGTTGAATA CTCATCTCT TCCTTTTCA ATATTATTGA AGCATTTATC AGGGTTATTG TCTCATGAGC GGATACATAT
 CCTTATTCCC GCTGTGCCCT TACAACCTAT GAGTATGAGA AGGAAAAAGT TATAATACT TCGTAATAAG TOCCAATAAC AGAGTACTCG CCTATGTATA
 5001 TTGAATCTAT TTAGAAAAAT AAACAAATAG GGGTTCCGCG CACATTTCCC CGAAAAGTGC CACCTGACGT CTAAGAAACC ATTATTATCA TGACATTAAAC
 AACTTACATA AATCTTTTTA TTTGTTTATC CCAAGGCGC GTGTAAAGG GCTTTTCAG GTGGACTGCA GATTCCTTGG TAATAANTAGT ACTGTAATTG
 5101 CTATAAAAAT AGGCGTATCA CGAGGCCCTT TCCTCTTCAA
 GATATTTTTA TCCGCATAGT GCTCCGGAA AGCAGAAGTT

FIG. 24C



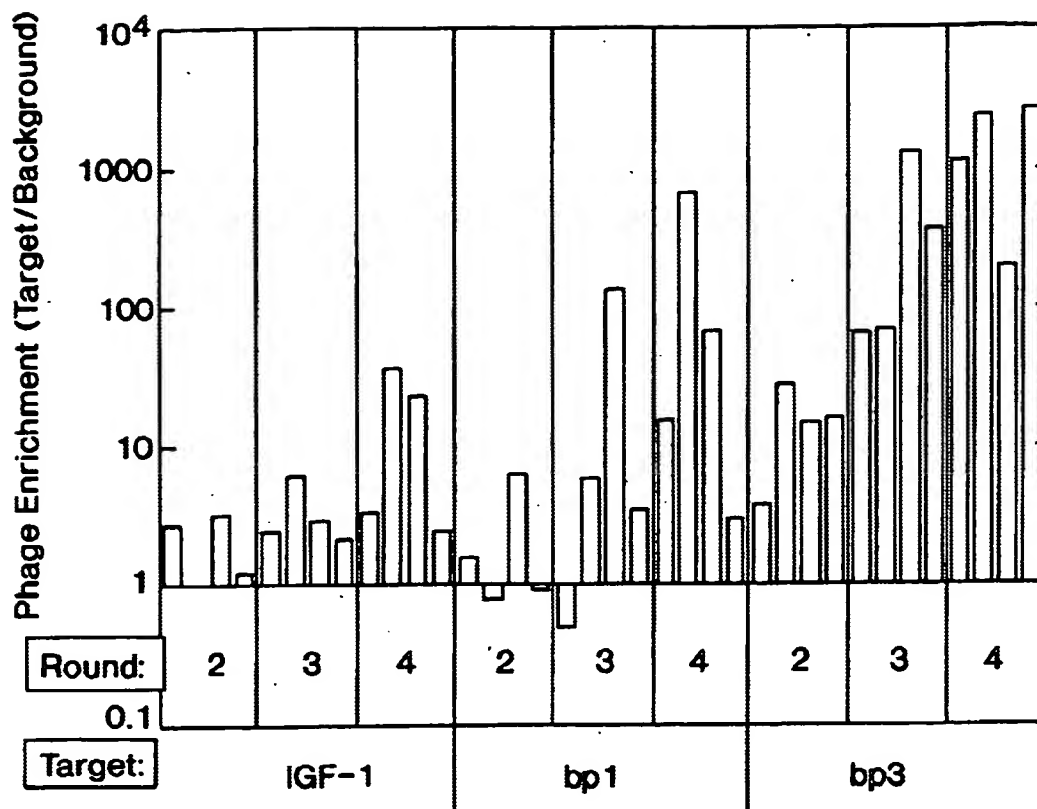


FIG. 25

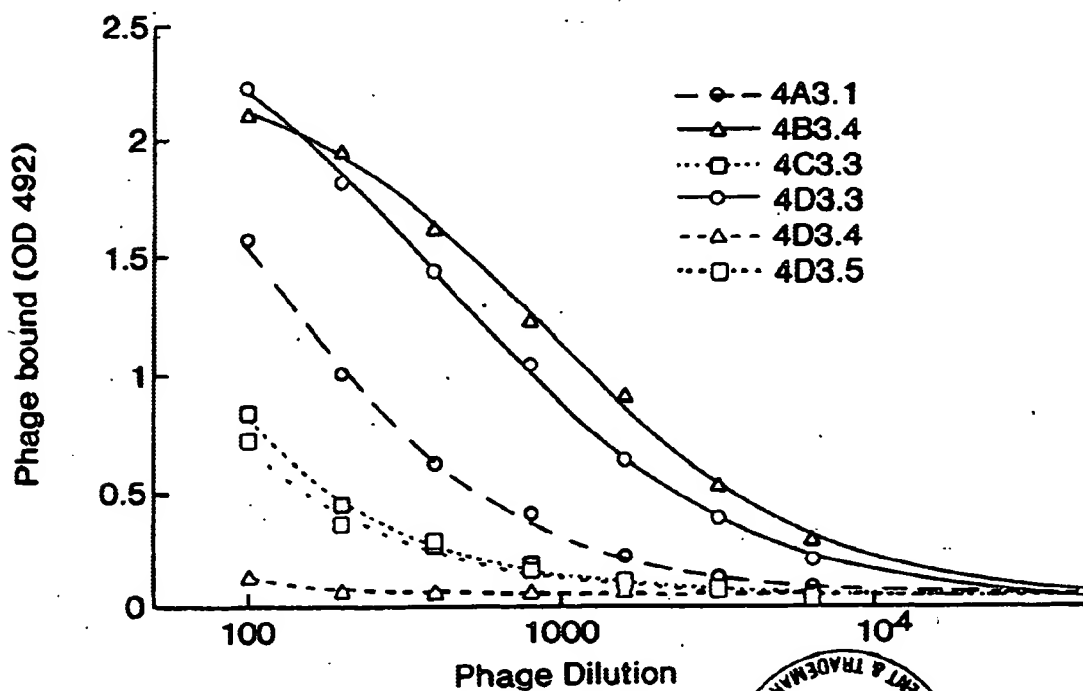


FIG. 26



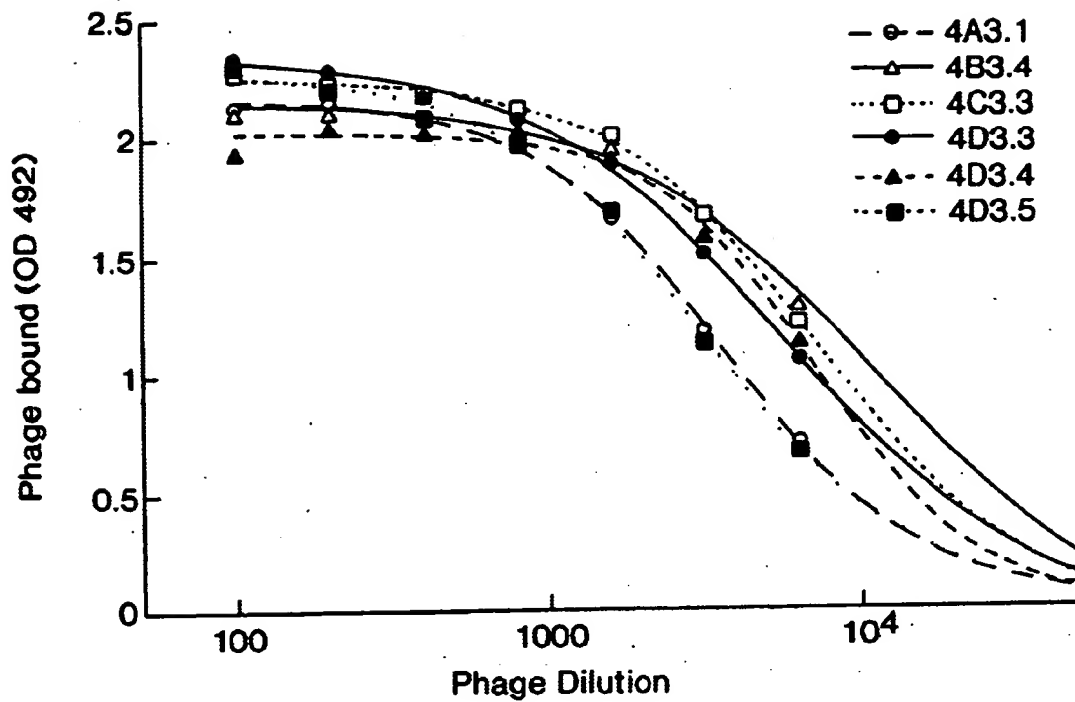


FIG. 27

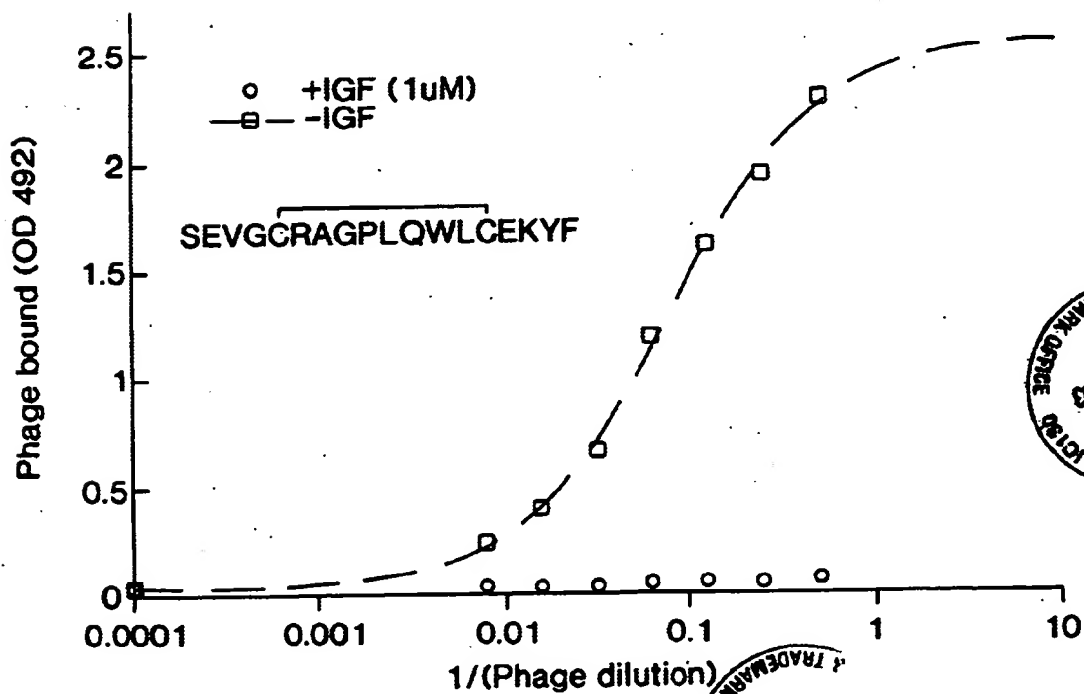


FIG. 28

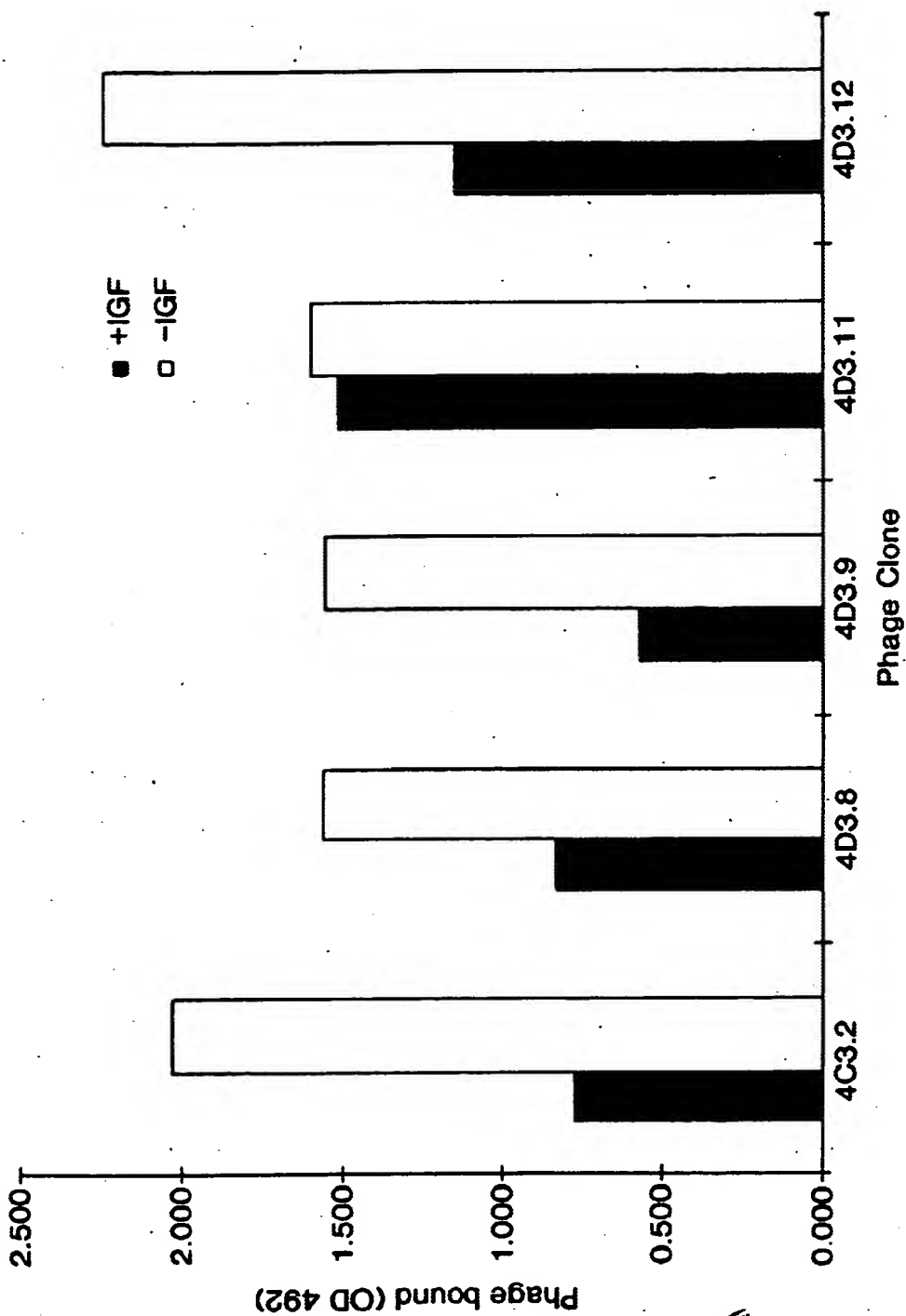
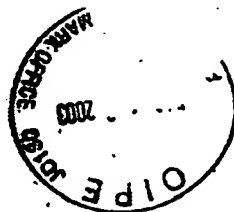


FIG. 29



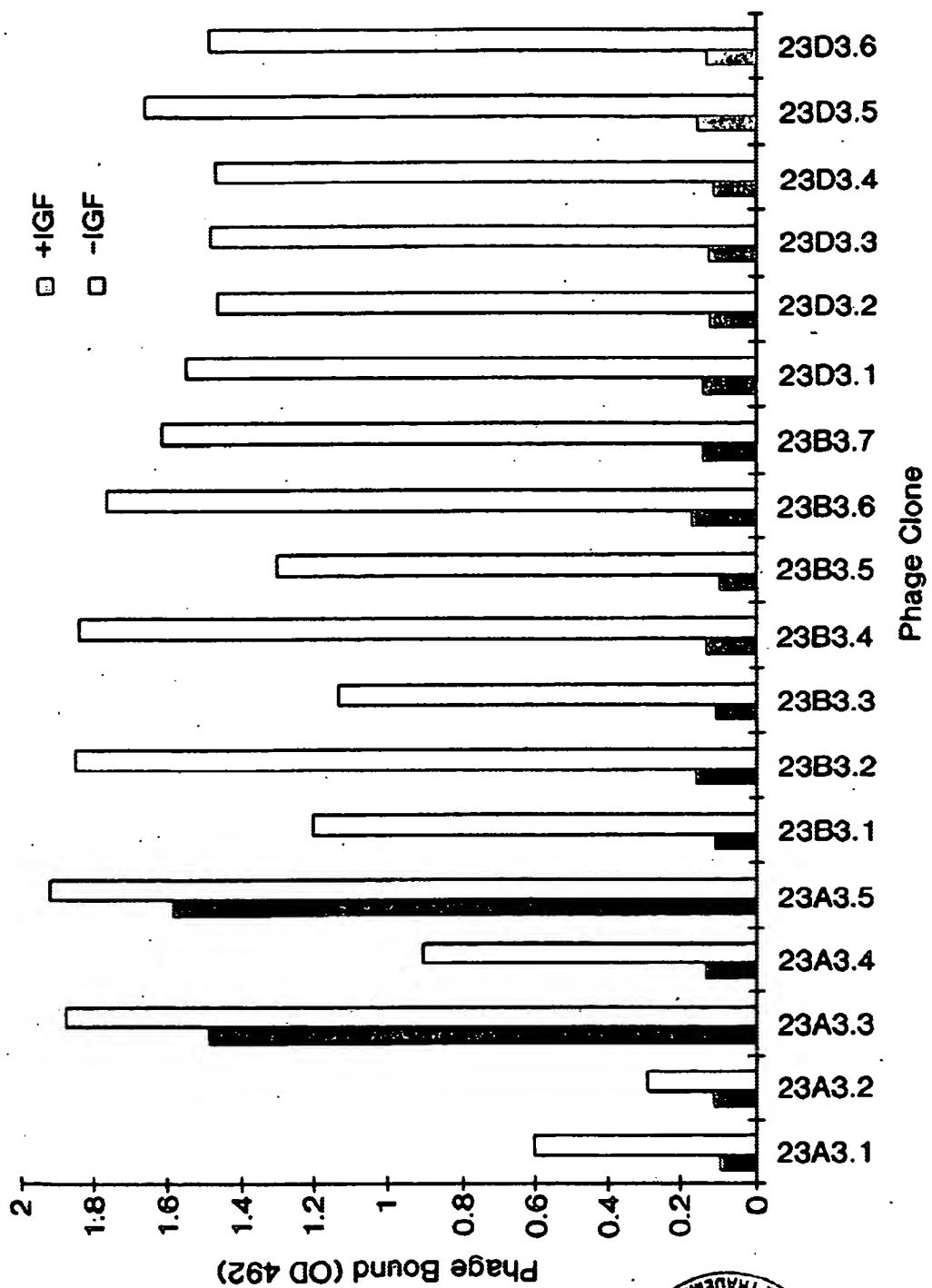
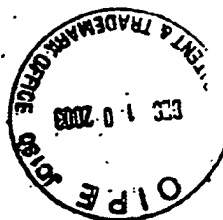


FIG. 30



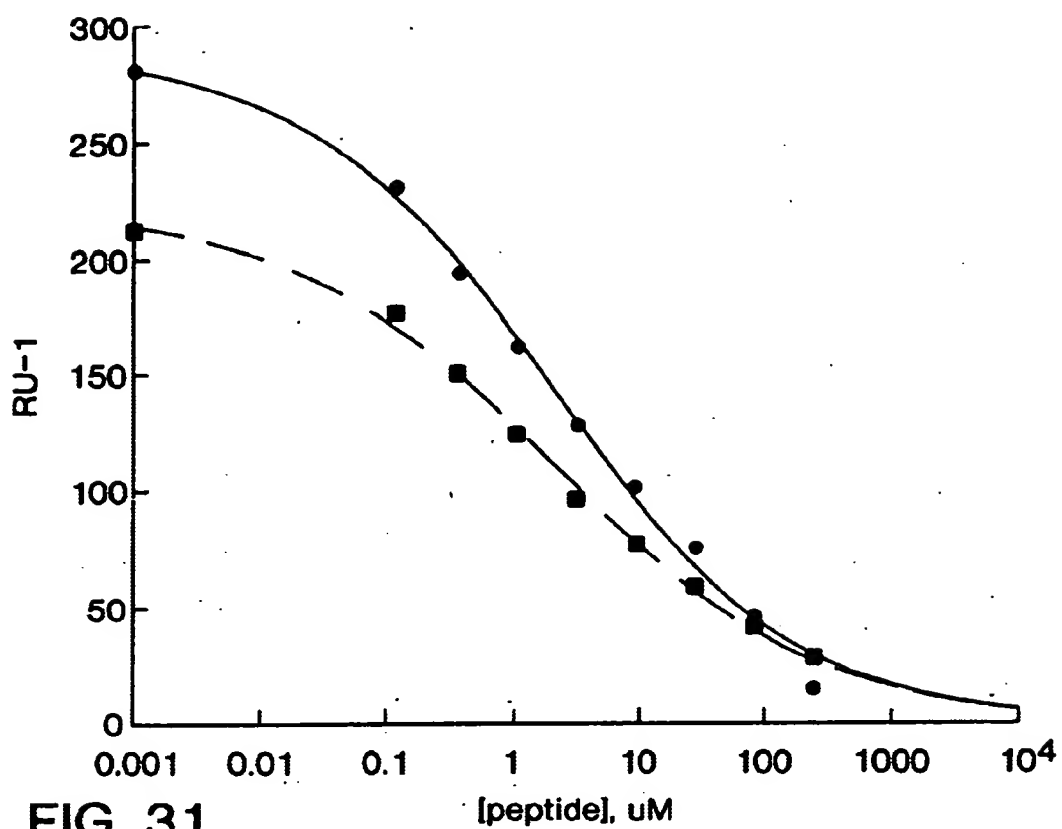


FIG. 31

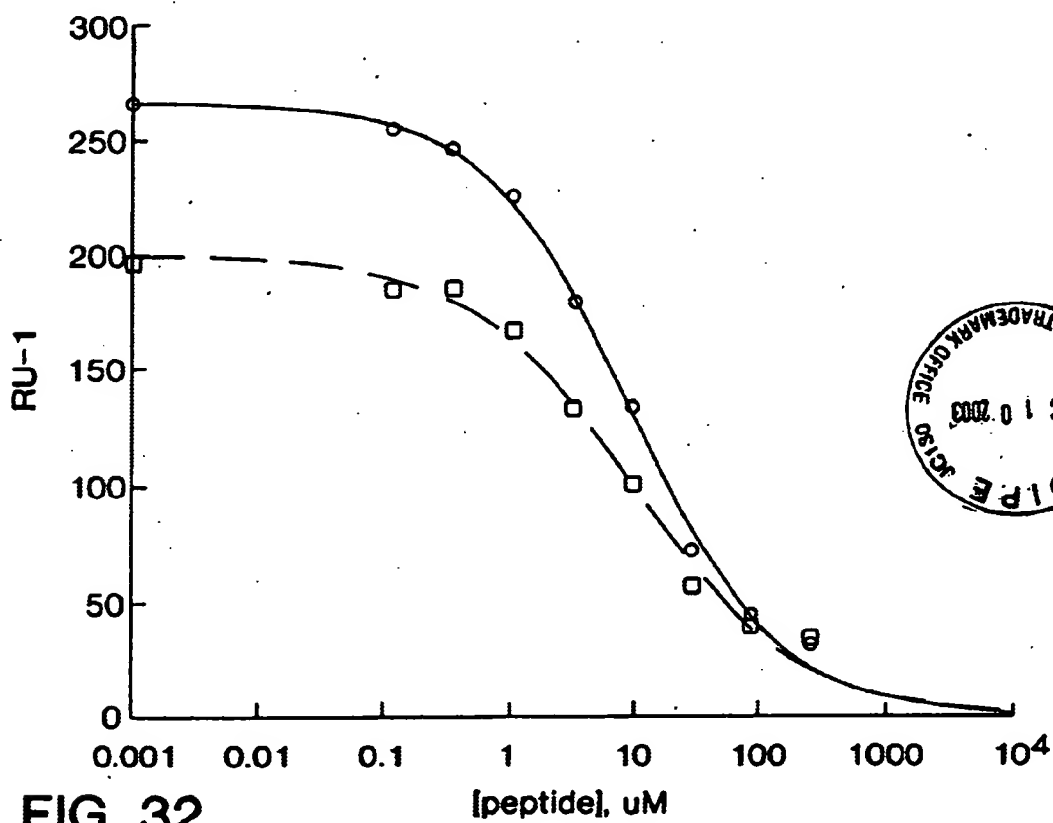


FIG. 32



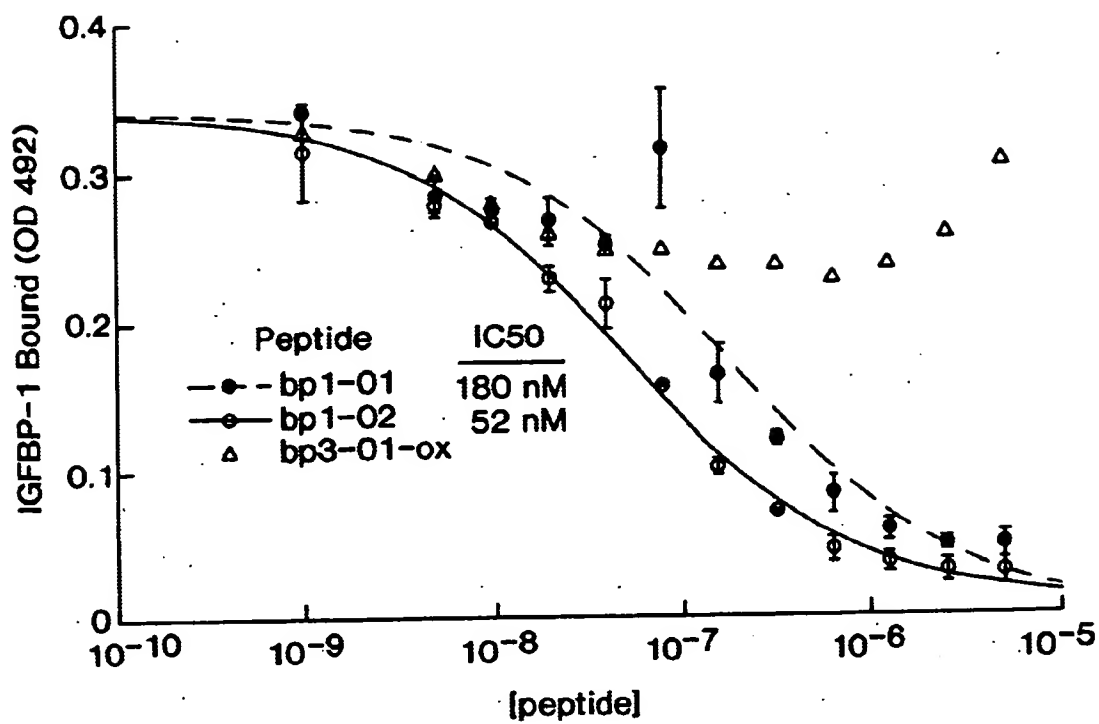


FIG. 33

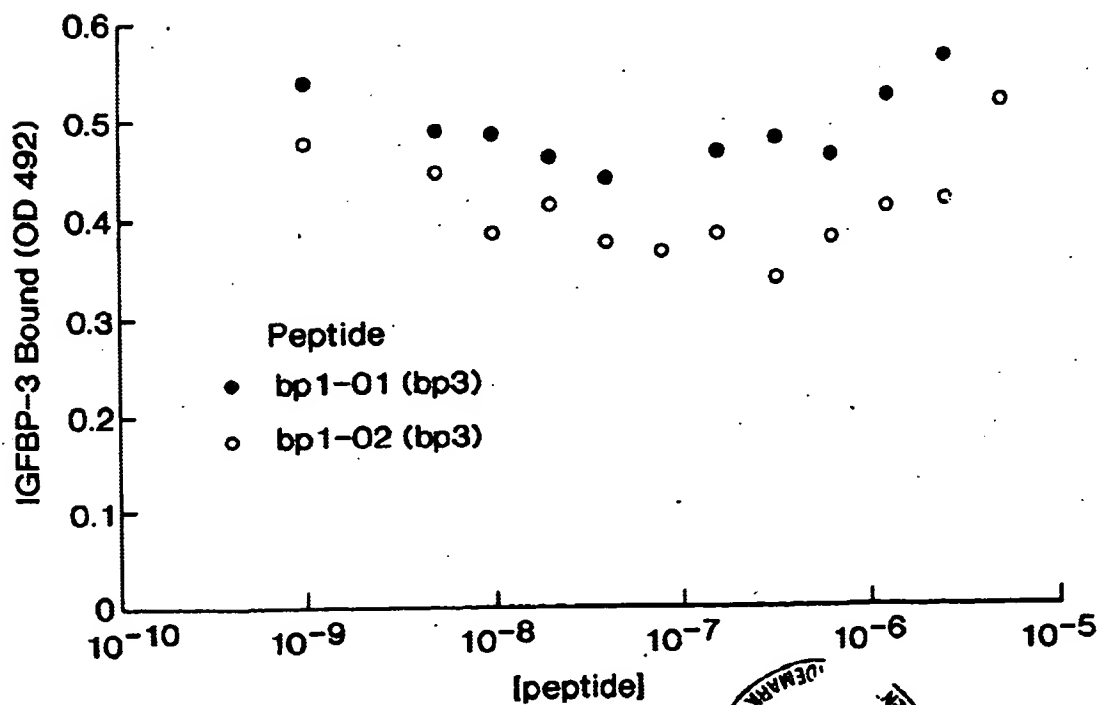


FIG. 34



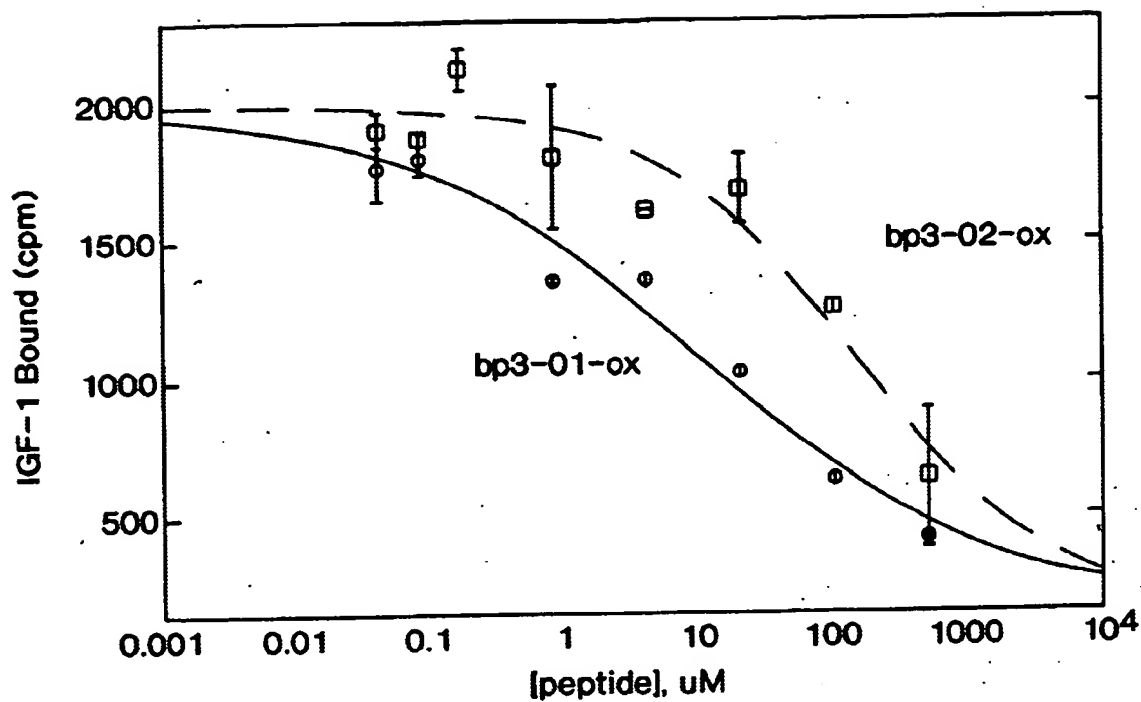


FIG. 35

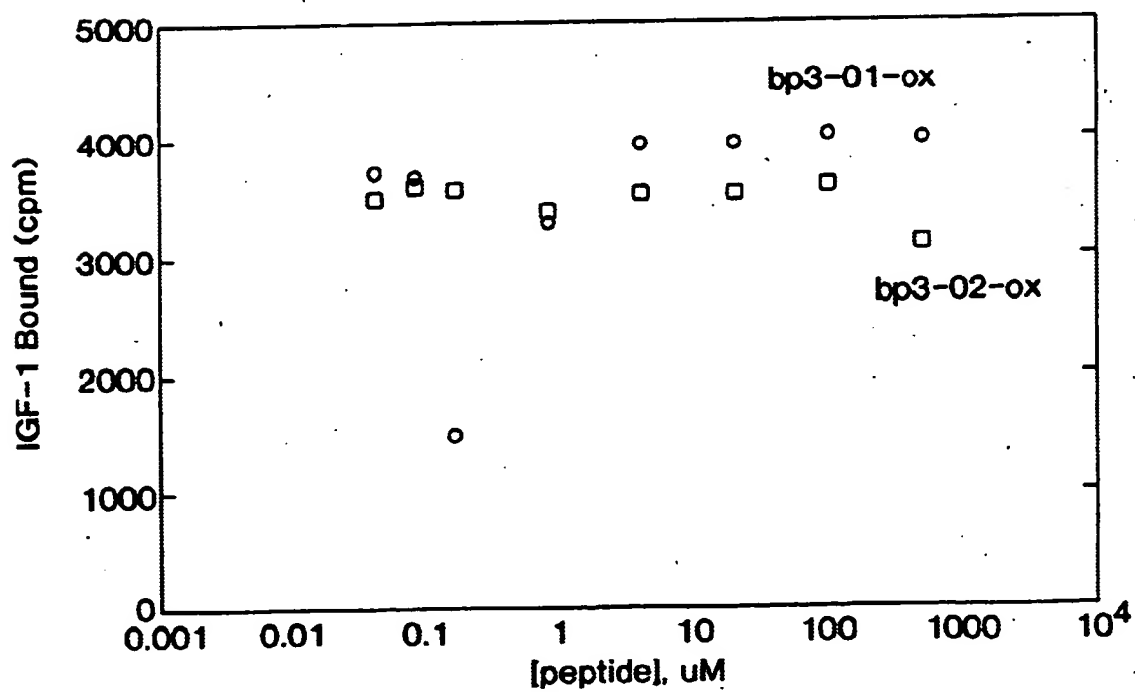


FIG. 36



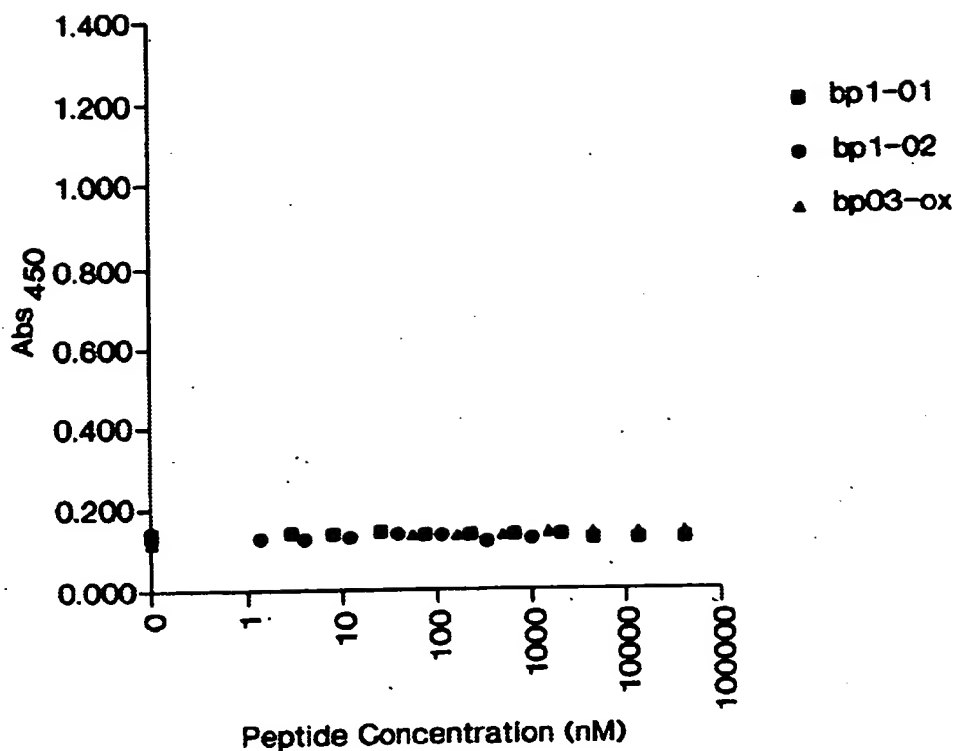


FIG. 37A

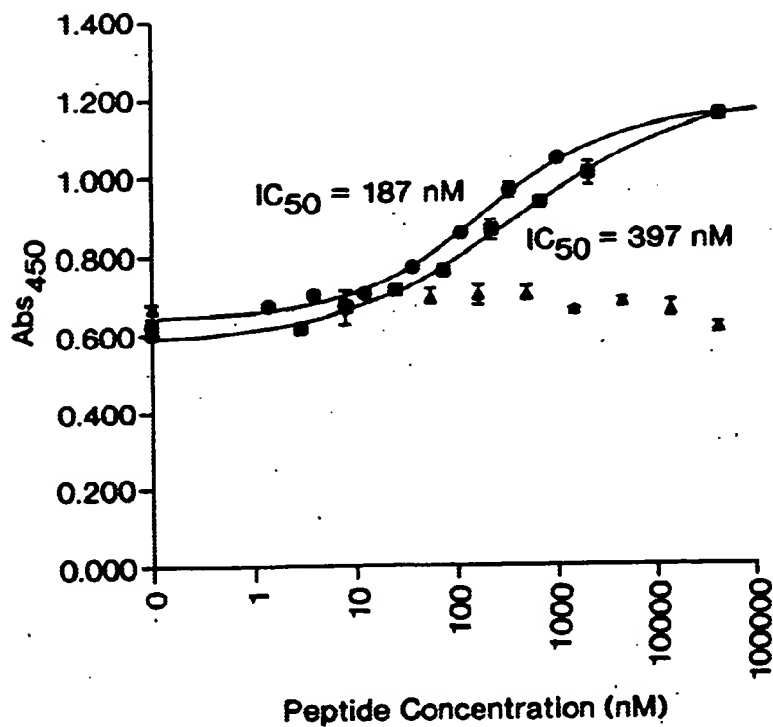


FIG. 37B



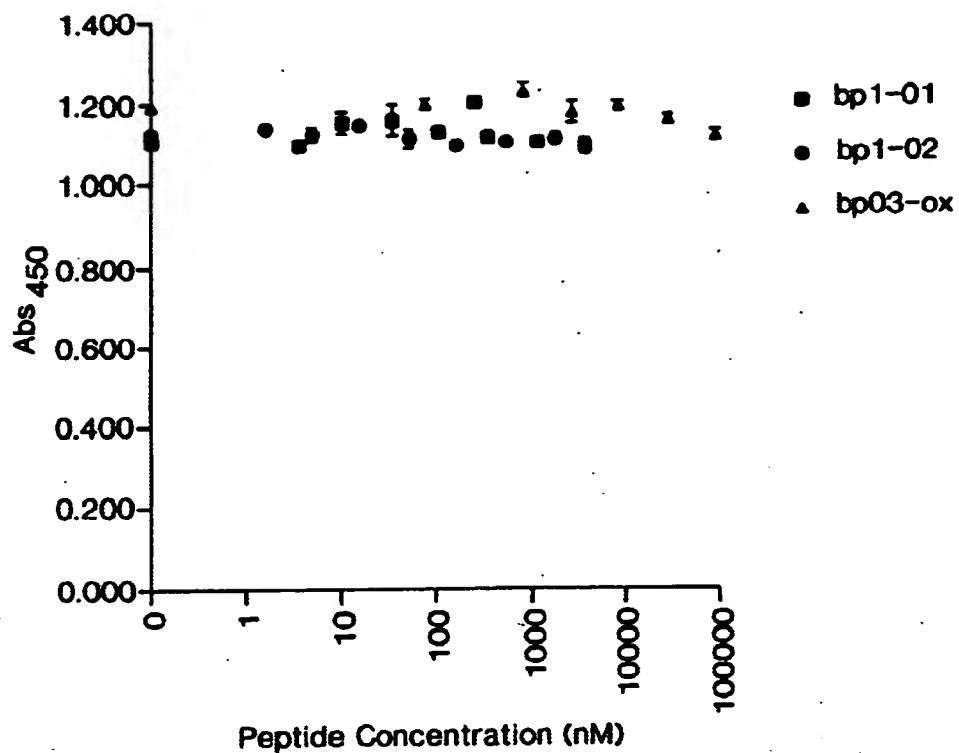


FIG. 37C

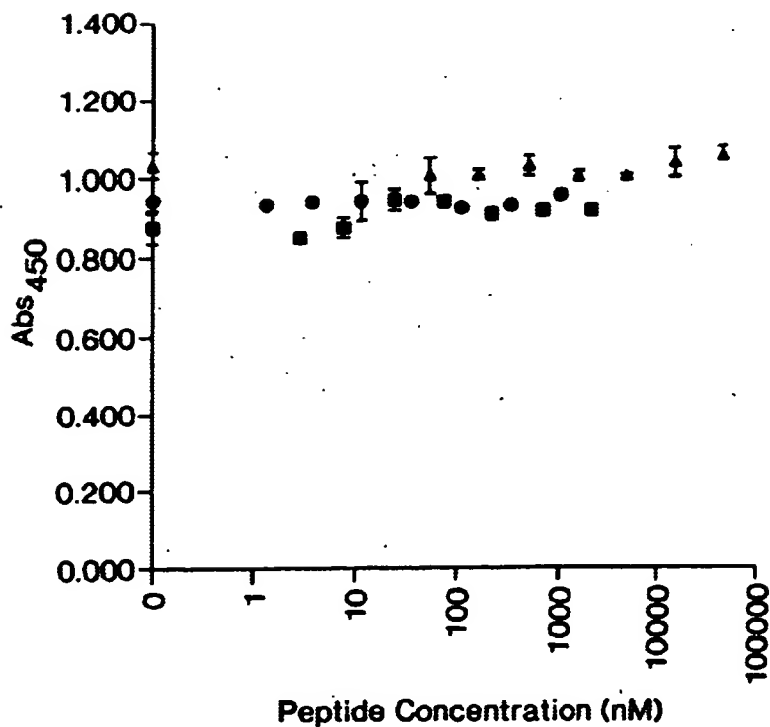


FIG. 37D



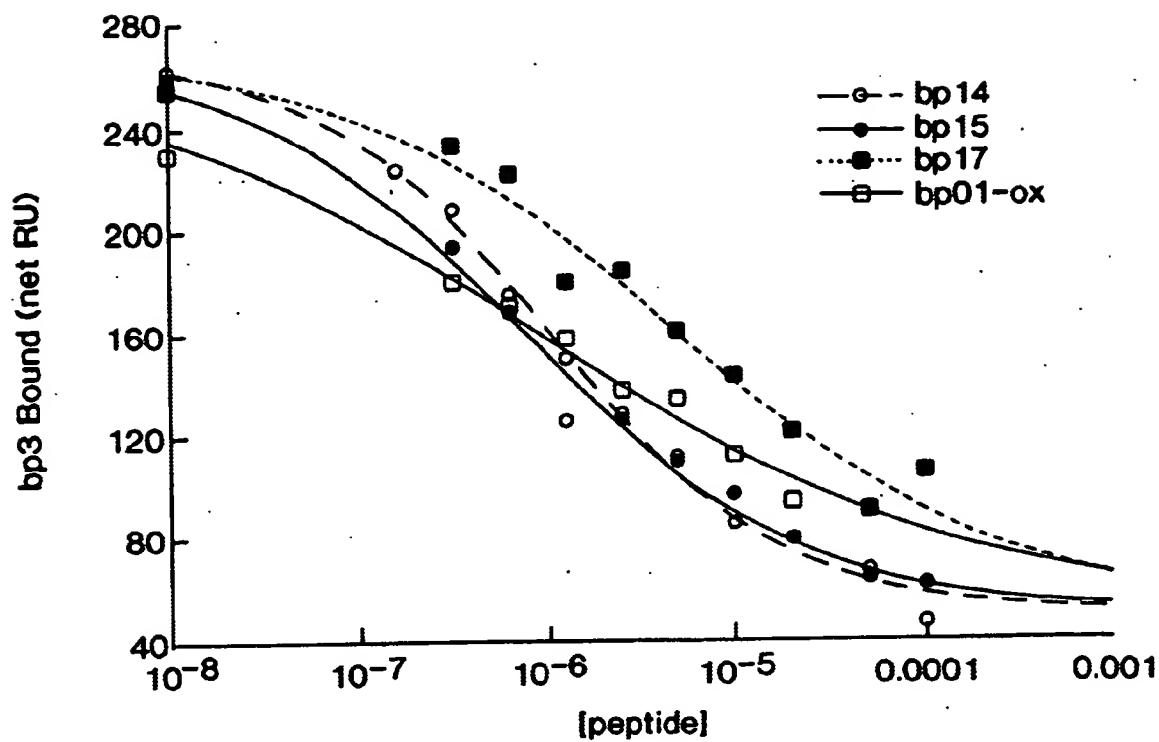


FIG. 38

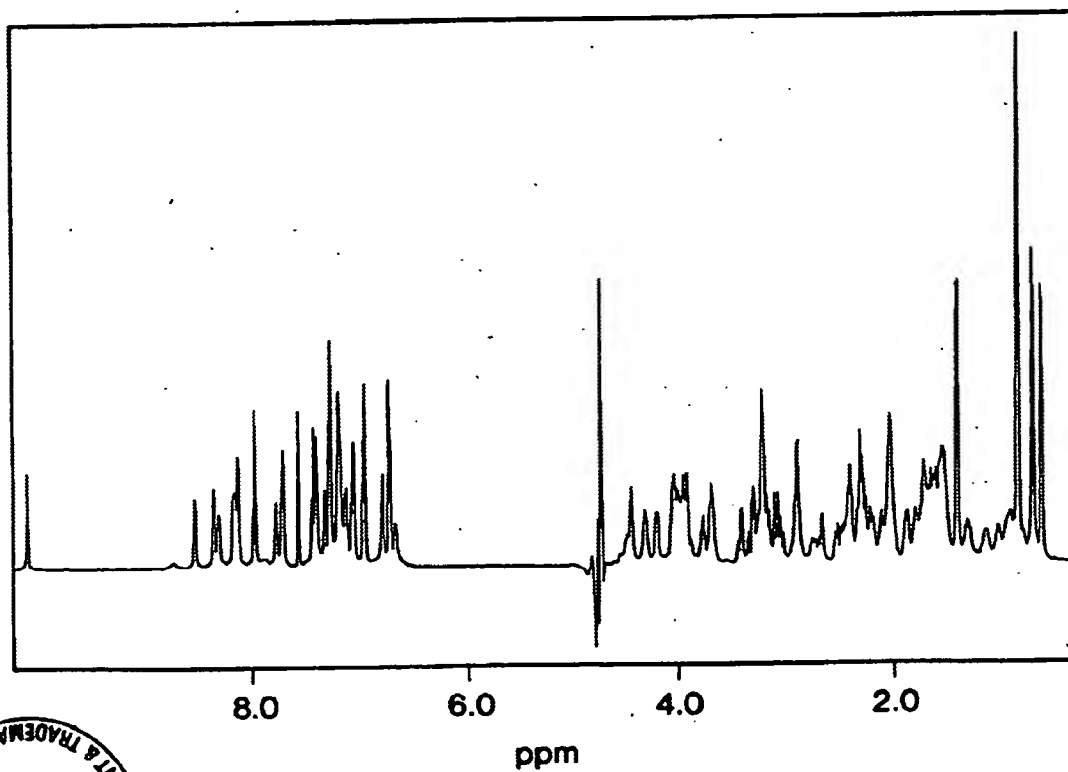


FIG. 39



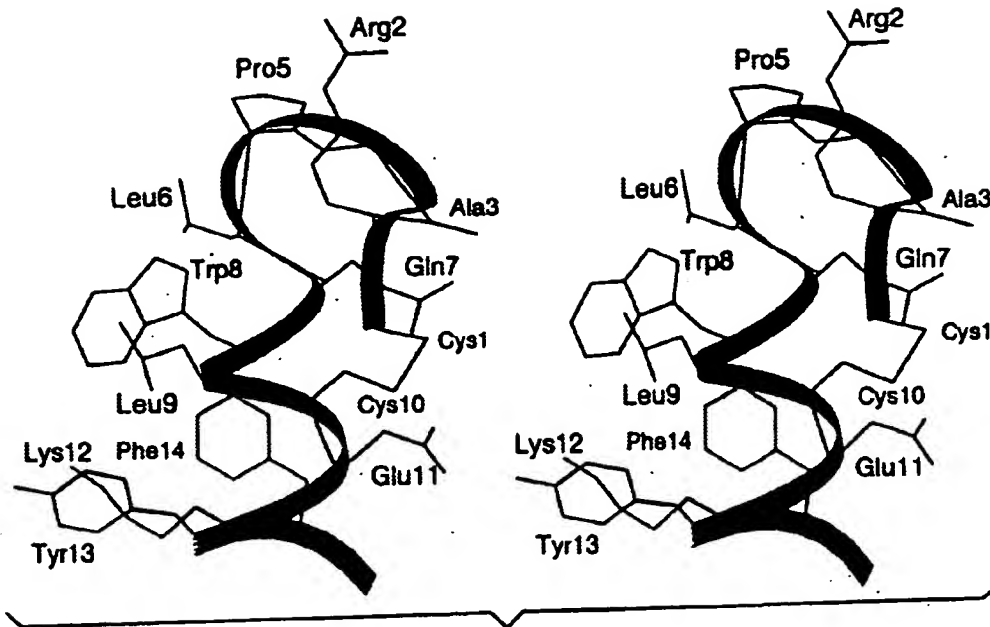


FIG. 40A

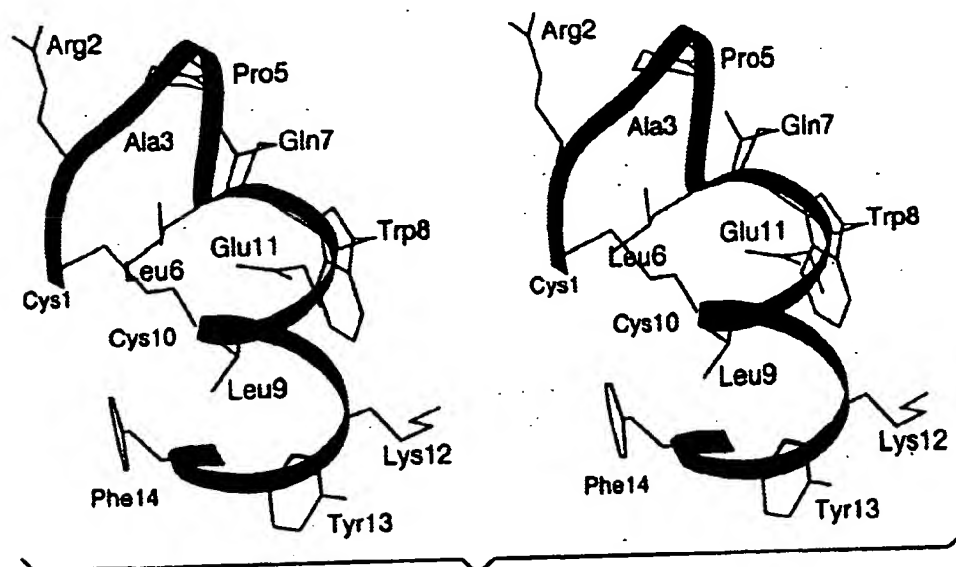


FIG. 40B



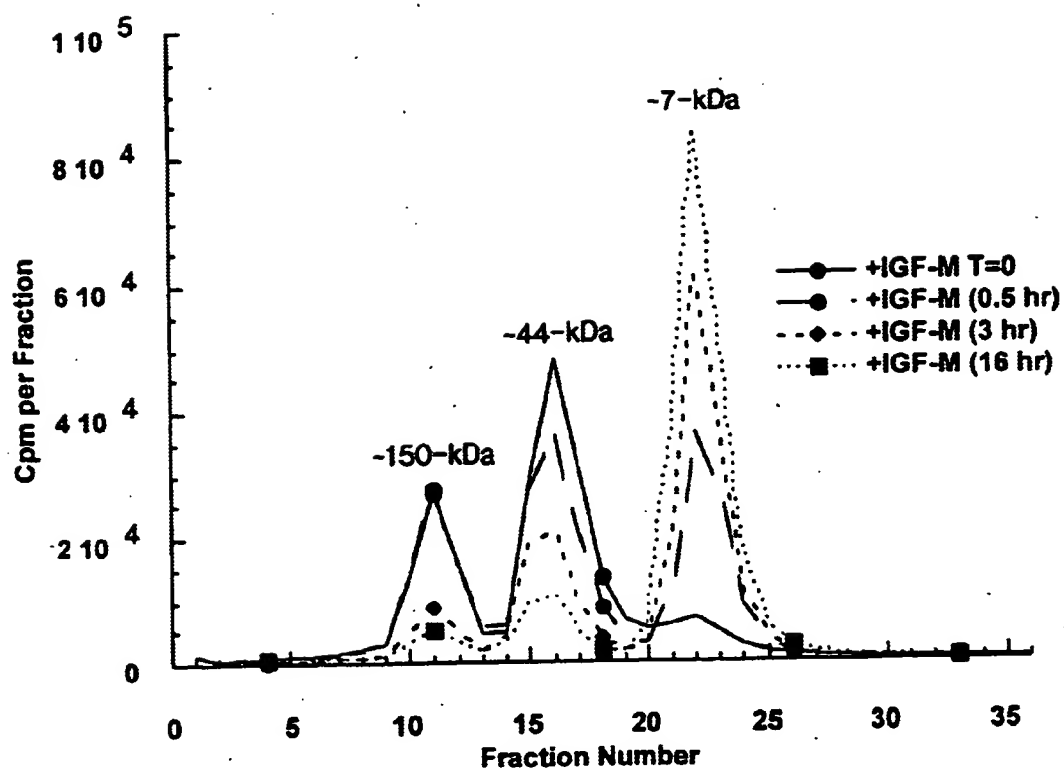
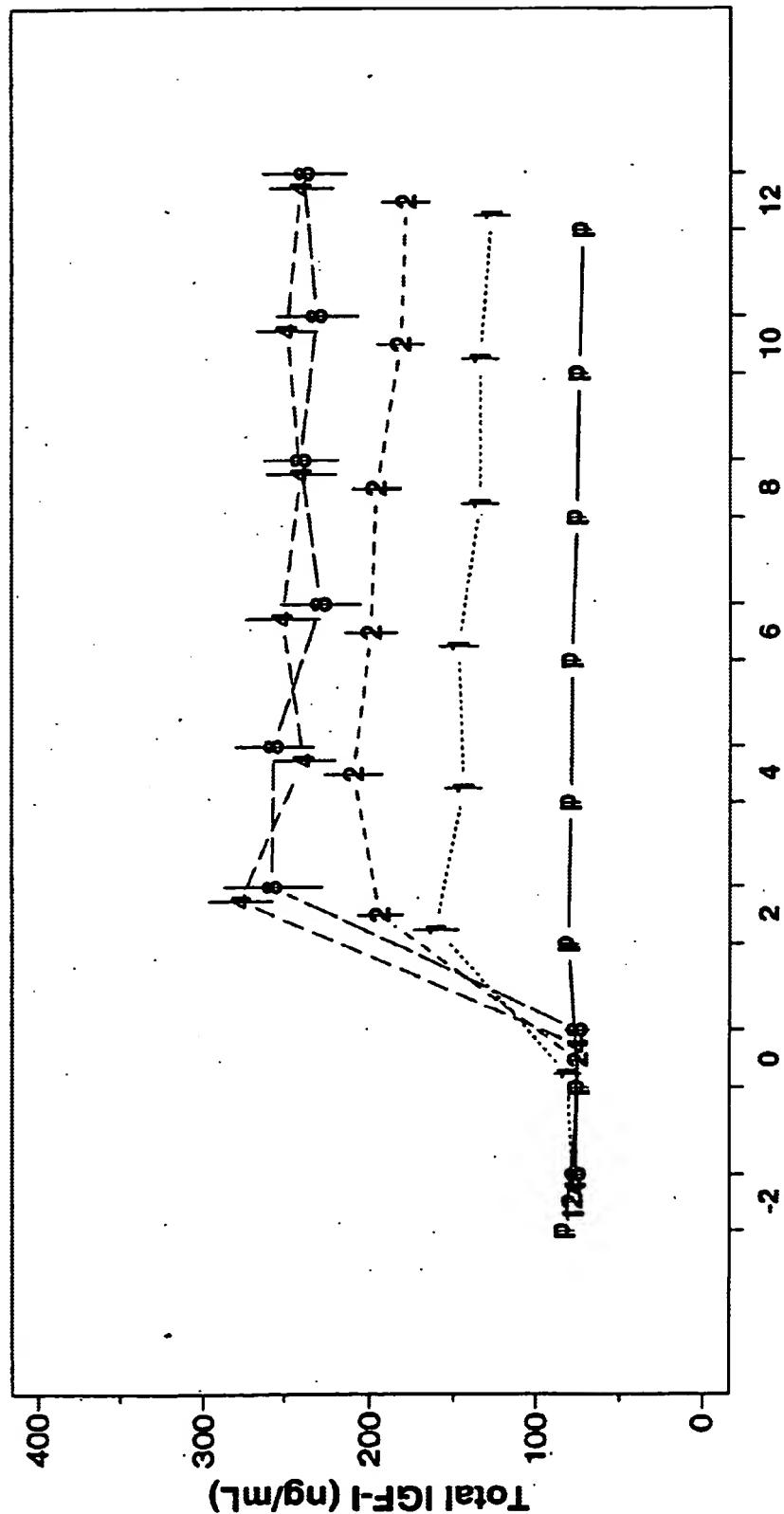


FIG. 41



Effect of IGF-I Treatment on Total IGF-I

(Mean \pm SE)

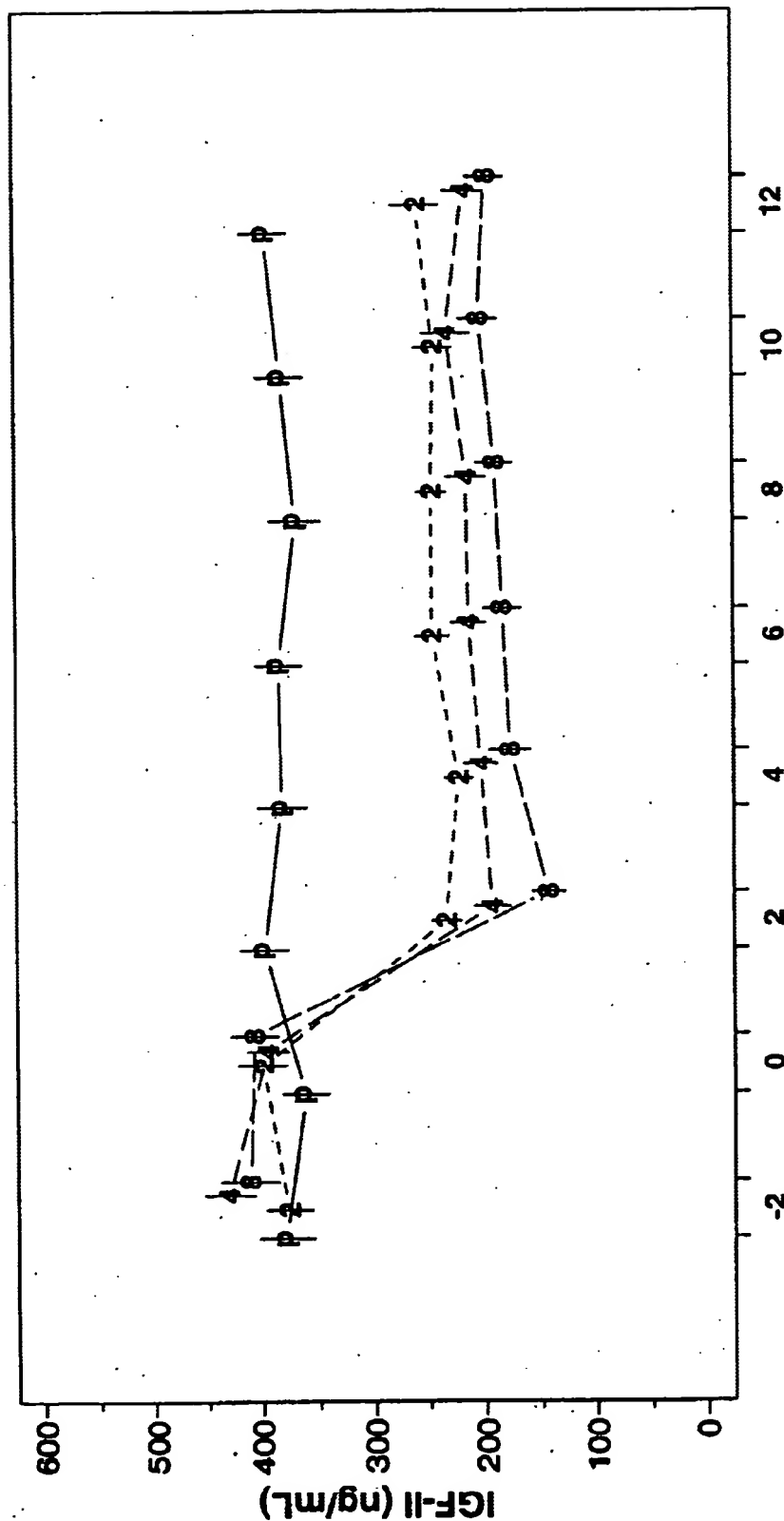


Treatment Visits (Week)

FIG. 42



Effect of IGF-I Treatment on IGF-II (Mean \pm SE)

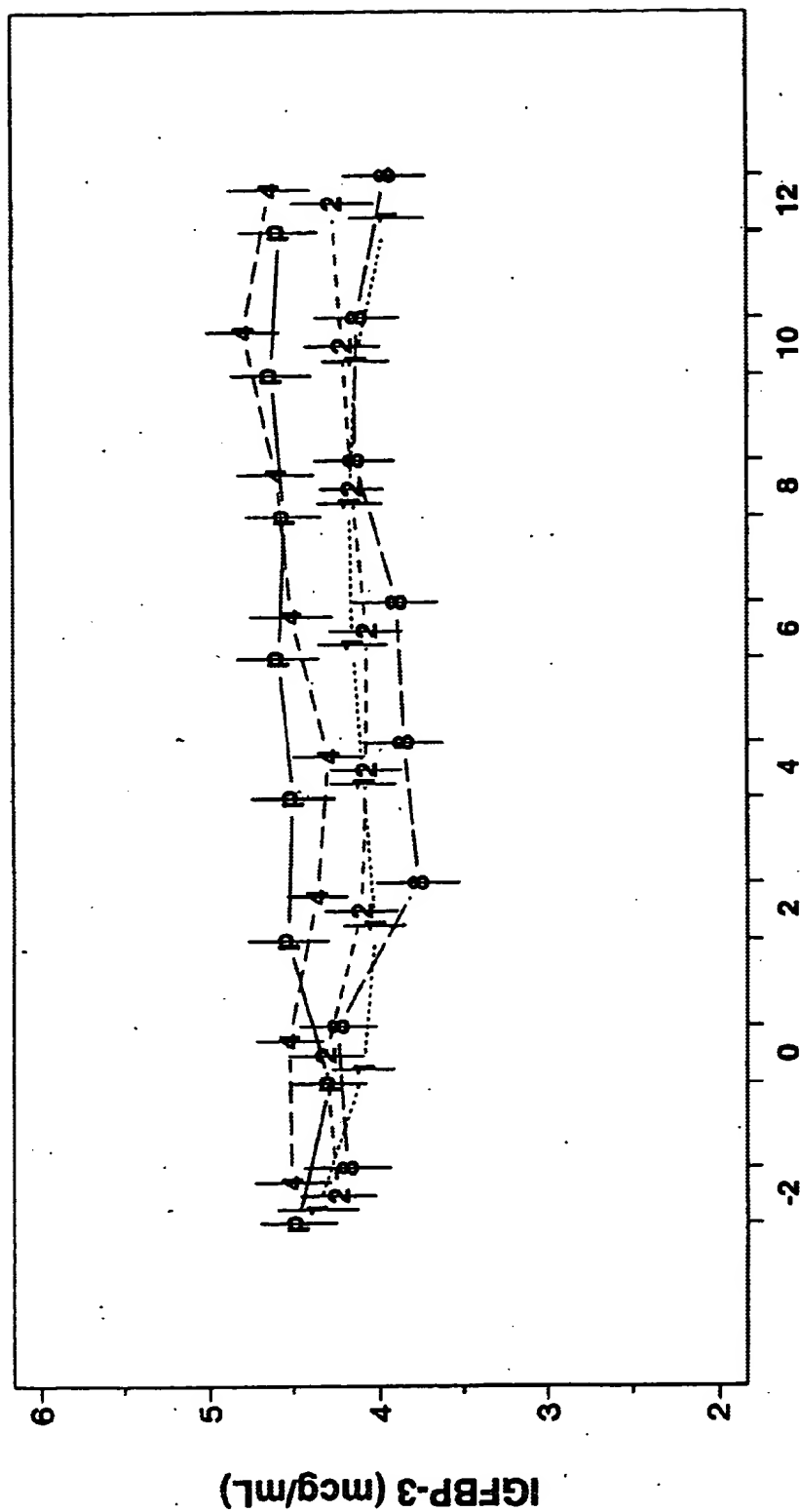


Treatment Visits (Week)

FIG. 43



Effect of IGF-I Treatment on IGFBP-3 (Mean \pm SE)



Treatment Visits (Week)

FIG. 44

